CLINICAL DIABETOLOGY

Clinical Diabetology (ISSN 2450–7458) is published six times a year by „Via Medica sp. z o.o." sp.k.
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Indexed in base of CAS, Index Copernicus (74.12), Ulrich's Periodicals Directory and in base of The Ministry of Science and Higher Education (10)

Za prenumeratę czasopisma „Clinical Diabetology" przysługuje 5 pkt edukacyjnych*

*na podstawie rozporządzenia Ministerstwa Zdrowia z dnia 6 października 2004 r. w sprawie sposobów dopełnienia obowiązku doskonalenia zawodowego lekarzy i lekarzy dentystów (Dz.U. 04.231.2326 z dnia 22 października 2004 r.)

2017 Guidelines on the management of diabetic patients

A position of Diabetes Poland

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Conflict of interest declaration of the Working Group members is available on the website: cukrzyca.info.pl

CLINICAL DIABETOLOGY

JOURNAL OF THE DIABETES POLAND

2017, Vol. 6, Suppl. A

DOI: 10.5603/DK.2017.0001

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The 2017 Diabetes Poland guidelines — remaining on the path of progress

Since 2005, the Diabetes Poland (PTD, Polskie Towarzystwo Diabetologiczne) prepares and publishes annually its guidelines on the management of diabetic patients. The idea of guideline development was first suggested in 2004 by Prof. Jacek Sieradzki who was the president of PTD at that time. The first chairperson of the PTD Guideline Writing Group was Prof. Władysław Grzeszczak who acted in this capacity in 2005–2011, followed by the next president of PTD, Prof. Leszek Czupryniak, in 2011–2015.

The guidelines are a product of a team of nearly 50 experts representing numerous medical specialties, covering all aspects of clinical diabetes care. Guideline chapters were prepared by teams coordinated by their leaders.

The goal of this expert teamwork is to improve prevention, diagnosis, and management of diabetes and its complications in Poland. The PTD guidelines reflect advances in diabetology, including new clinical and experimental study findings, epidemiological observations, and registry data. Thus, some modifications and novel aspects appear every year. However, as the guidelines have always been based on the principles of evidence-based medicine, only minor changes are required, related to new knowledge from reliable research with major implications for clinical practice.

In line with the principles of evidence-based medicine, levels of evidence underlying the recommendations have been introduced in some chapters of the 2017 PTD guidelines, similarly to the American Diabetes Association (ADA) guidelines.

Summary of the most important changes to the 2017 PTD guidelines

In Chapter 1, the contents has been rearranged and the approach to the diagnosis of hyperglycemia has been simplified. If no symptoms of hyperglycemia are present and random venous blood glucose is ≥ 200 mg/dL (11.1 mmol/L), fasting venous blood glucose ≥ 126 mg/dL (≥ 7.0 mmol/L) on one and not two occasions is now sufficient for the diagnosis of diabetes.

In Chapter 3 on glycemia monitoring, new information has been added regarding flash glucose monitoring (FGM).

In Chapter 4 on the treatment goals, the target HbA_{1c} level in women with prepregnancy diabetes contemplating pregnancy has been set more liberally at < 6.5% (48 mmol/mol), in accordance with the opinion of other diabetes societies (ADA, National Institute for Health and Care Excellence — NICE), while HbA_{1c} level < 6.0% (42 mmol/mol) remains the goal in the second and third trimester, if it is not associated with an increased rate of hypoglycemia. Recommendation on target lipid levels have been expanded based on the available evidence. The treatment goal in diabetic subjects at very high cardiovascular risk is low-density lipoprotein cholesterol (LDL-C) level < 70 mg/dL (1.9 mmol/L) or reduction by at least 50% if baseline LDL-C level is 70–135 mg/dL (1.9–3.5 mmol/L), and LDL-C level < 100 mg/dL (2.6 mmol/L) or reduction by at least 50% if baseline LDL-C level is 100–200 mg/dL (2.6–5.2 mmol/L) in diabetic subjects at high cardiovascular risk. In subjects at low or moderate cardiovascular risk, defined as subjects < 40 years of age with diabetes type 1 but without chronic complications and other cardiovascular risk factors), the goal LDL-C level is < 115 mg/dL (3.0 mmol/L). A secondary goal for lipid-lowering treatment is non-high-density lipoprotein cholesterol (non-HDL-C) level, also set in relation to the overall cardiovascular risk at < 100 mg/dL (2.6 mmol/L) in diabetic subjects at very high cardiovascular risk, < 130 mg/dL (3.4 mmol/L) in subjects at high cardiovascular risk, and at < 145 mg/dL (3.7 mmol/L) in subjects at low to moderate cardiovascular risk.

In Chapter 5 on the organization of care for patients with diabetes, recommendations have been added regarding care for patients with diabetic foot syndrome. This care should be provided by referral diabetes foot clinics (one per voivodship) and basic care clinics (the number depending on the population of given voivodship) that cooperate with referral clinics. Personnel requirements were set, as were the principles of multispecialty care, equipment requirements, access to laboratory and microbiological testing, and opportunities for hospital care.

In Chapter 6, multiple small editorial changes have been made, and the nomenclature has been improved. The need for individualized nutrition care has been highlighted. Recommendations regarding carbohydrate and protein intake have been clarified. Carbohydrates should provide about 45% of the total calorie intake; and if they are consumed in the form of low glycemic index and high fiber content products, their share in the total calorie intake may be even higher (up to 60%). High caloric intake from carbohydrates should also be a feature of the diet in subjects who are very active physically. In contrast, a lower carbohydrate share in the total calorie intake

(25–45%) may be temporarily recommended in patients with little physical activity if it cannot be significantly increased, e.g., due to concomitant conditions. In most diabetic patients, proteins should provide 15–20% of the total calorie intake (about 1–1.5 g/kg body weight/day). In patients with diabetes type 2 and excessive body weight, a low-calorie diet may contain 20–30% of protein. In patients with chronic kidney disease, protein intake should be about 0.8–1 g/kg body weight/day. Salt intake from all sources should not exceed 5 g per day.

In Chapter 8, recommendations regarding education have been updated, reflecting, among others, the technological progress in blood glucose monitoring.

In Chapter 9 on the management of diabetes type 1, use of insulin analogs for insulin therapy has been preferred based on the robust available evidence.

In Chapter 10, data from large randomized clinical trials have been included that indicate a reduction of total and cardiovascular mortality with the use of GLP-1 agonists and SGLT-2 inhibitors. The algorithm for drug treatment of diabetes type 2 has also been modified, with expanded options of insulin therapy intensification.

In Chapter 11, recommendations on initiating insulin therapy regardless of blood glucose levels have been clarified, which apply to all autoimmune-mediated diabetes types regardless of age and not only LADA, and not all but only warranted patient wishes. When glycemic control is reevaluated, insulin doses should be gradually increased by 2–4 units and not 4–8 units as recommended previously. In patients treated with single basal insulin injection, intensification of insulin therapy has been recommended when the basal insulin dose exceeds 30 units per day (10 units less compared to the previously recommended threshold). The recommended approaches to treatment intensification include adding rapid-acting insulin before meals, with possible stepwise intensification using the basal-plus approach, or alternatively initiation of mixed insulin therapy. A recommendation has been delated regarding insulin therapy using three or more insulin injections per day if the daily insulin requirement exceeds 80 units.

In Chapter 13 on the approach to treatment of dyslipidemia in 2016, the target LDL-C level < 70 mg/dL has been set for all patients with diabetes type 2. The target LDL-C level < 100 mg/dL has been only left in young patients with diabetes type 1 without other cardiovascular risk factors. New clinical trial results and metaanalyses of these studies have resulted in updated European Society of Cardiology (ESC) recommendations on the treatment of dyslipidemia that have also been adopted by PTD. With the perceived need for more treatment individualization in diabetic patients, target LDL-C and non-HDL-C levels set in the 2017 PTD guidelines vary, primarily in relation to the 10-year cardiovascular mortality risk. This risk is defined as very high in diabetes with concomitant cardiovascular disease (previous myocardial infarction, acute coronary syndrome, coronary revascularization or other revascularization procedures, stroke, transient ischemic attack, aortic aneurysm, and peripheral arterial disease) or other cardiovascular risk factors, i.e. albuminuria, hypertension, hypercholesterolemia, smoking, or a family history of cardiovascular disease. Patients without chronic diabetes complications and other cardiovascular risk factors are at high cardiovascular risk. Only in young patients with diabetes type 1 without chronic diabetes complications and other cardiovascular risk factors, the risk is moderate or low. Depending on the risk category, target LDL-C and non-HDL-C levels in the very high, high, and moderate to low risk groups are < 70 mg/dL and < 100 mg/dL, < 100 mg/dL and < 130 mg/dL, and < 115 mg/dL and < 145 mg/dL, respectively. In this way, we hope to increase implementation of these guidelines in the clinical practice.

In Chapter 14, it has been highlighted in the section on the management of a prolonged hypoglycemic episode that this situation may occur with all diabetes types and not only in diabetes type 2.

In Chapter 15, data have been updated on the mortality due to diabetic ketoacidosis which is now estimated at 0.2–2%, and not 5% as indicated previously, and depends on such factors as the expertise of the treating team. Recurrent episodes of diabetic ketoacidosis are associated with a much higher mortality risk. Regarding the diagnosis of diabetic ketoacidosis, a comment has been added that in patients treated with SGLT-2 inhibitors, blood glucose values may be lower than the definition given (> 250 mg/dL). As commercial hypotonic 0.45% saline solution is now available, it has again been recommended in the treatment of hyperglycemic-hyperosmolar state.

In Chapter 21 on the organization of care for patients with diabetes foot syndrome, the organizational structure of referral diabetes foot clinics (previously regional multi-specialty diabetes foot clinics) and basic care clinics (previously diabetes foot service in diabetology clinics) has been described, aiming to improve the diagnosis and treatment of diabetes foot syndrome in Poland. The recommendation regarding diagnostic tests for osteitis has been clarified, and the interval between follow-up foot X-rays has been defined as every 3 to 6 weeks.

Numerous editorial corrections have been made in Chapter 22. Target blood pressure values have been defined as < 130/85 mm Hg in those aged 16 years or above, while percentile charts remain in use in younger age groups. When discussing insulin therapy, a recommendation has been added that the magnitude of the basal dose and

its profile should depend on the age of the child and the type of insulin pump. Recommendations regarding insulin injections with meals have been clarified, and it has been indicated that in the youngest children, in whom planning the timing and size of the meal is not possible, dose splitting may be considered by administering half of the dose before a meal and the other half during or after a meal. Additions and modifications related to continuous glucose monitoring have been added to the recommendations regarding blood glucose self-monitoring. Important changes have been made to the Table 22.1 on the recommended intervals between serum lipid profile, albuminuria, serum creatinine, urinalysis, and thyroid function tests, as performance of these tests is now recommended every 1–2 years at the discretion of the treating physician.

In Chapter 23, significant changes have been made regarding the target 1-hour post-prandial blood glucose self-monitoring value which has been relaxed from 120 to 140 mg/dL. The target HbA_{1c} level in the first trimester in women with prepregnancy diabetes has been specified at < 6.5% (48 mmol/mol). Nutritional recommendations have been amended, including the recommended protein intake of 1.3 g/kg of body weight, and the recommended saturated fatty acid intake of less than 10% of the total energy value of the diet. Due to the fact that oral glucose-lowering agents pass through the placenta and no studies are available regarding their long-term effects in the offspring, no recommendation for metformin use during pregnancy has been upheld.

In Chapter 25, recommendations regarding glucose, insulin, and potassium infusion in adult diabetic patients in the perioperative period have been unified and simplified, and a section on differences regarding the management of children has been added.

A new Chapter 30 has been added to the 2017 PTD guidelines, with brief recommendations regarding selected special situations in diabetic patients, including shift work, time zone change, and glucocorticosteroid therapy.

In Appendix 4, errors regarding the management of diabetes type 1 in relation to the TPOAb titer have been corrected.

In Appendix 6 which includes recommendations regarding the principles of personal insulin pump therapy reimbursed by the National Health Fund in children, adolescents, and young adults below 26 years of age, the requirements for centers contracting this service have been clarified, which include patient education regarding continuous subcutaneous insulin infusion, providing the patient with an insulin pump, and offering consultation services. In case of insulin pumps with continuous glucose monitoring option, alarm presetting is recommended, taking into account the current level of metabolic control and patient capabilities. Patient knowledge should be verified using a diabetes knowledge test developed by PTD. The HbA_{1c} level criterion for insulin pump therapy reimbursement has been changed from > 9.0% to ≥ 9.0%.

By making the above changes, in part suggested by the users of these recommendations, the 2017 PTD Guideline Writing Group hopes that these guidelines will serve as an even better signpost leading to improved medical care for diabetic patients in our country.

We sincerely thank everybody who has contributed to the development of the new edition of PTD guidelines!

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Table 1. American Diabetes Association evidence-grading system for "Standards of Medical Care in Diabetes"

Level of evidence	Description
A	Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including: • Evidence from a well-conducted multicentre trial • Evidence from a meta-analysis that incorporated quality ratings in the analysis Compelling nonexperimental evidence, i.e., "all or none" rule developed by the Centre for Evidence--Based Medicine at the University of Oxford Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including: • Evidence from a well-conducted trial at one or more institutions • Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	Supportive evidence from well-conducted cohort studies • Evidence from a well-conducted prospective cohort study or registry • Evidence from a meta-analysis of cohort studies Supportive evidence from well-conducted case-control study
C	Supportive evidence from poorly or incontrolled studies • Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results • Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls) • Evidence from case series or case reports Conflicting evidence with the weight of evidence supporting the recommendation
E	Expert consensus or clinical experience

1. Diagnostic criteria for dysglycemia

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia due to defective secretion and/or action of insulin. Chronic hyperglycemia is associated with damage, dysfunction, and failure of various organs, in particular eyes, kidneys, nerves, heart, and blood vessels.

I. Symptoms suggesting the presence of diabetes:

— Body weight reduction;
— Increased thirst;
— Polyuria;
— Fatigue and somnolence;
— Presence of purulent skin lesions and inflammatory conditions of the genitourinary tract.

In case of the onset of symptoms random venous plasma glucose level should be measured (table 1.1).

II. Diagnostic criteria for dysglycemia (table 1.1):

— Random venous plasma glucose level measurement at the time when symptoms of hyperglycemia are identified — values ≥ 200 mg/dL (≥ 11.1 mmol/L) are consistent with the diagnosis of diabetes;
— If no symptoms are present or when symptoms are present and random blood glucose is < 200 mg/dL (< 11.1 mmol/L), fasting blood glucose should be measured twice on separate days — diabetes is diagnosed if fasting blood glucose on both these occasions is ≥ 126 mg/dL (≥ 7.0 mmol/L);
— If no symptoms of hyperglycemia are present and random blood glucose is ≥ 200 mg/dL (≥ 11.1 mmol/L), fasting blood glucose should be measured and diabetes is diagnosed if fasting blood glucose is ≥ 126 mg/dL (≥ 7.0 mmol/L);
— An oral glucose tolerance test (OGTT) should be performed if fasting blood glucose on one or two occasions is 100–125 mg/dL (5.6–6.9 mmol/L), or impaired glucose tolerance (IGT) or diabetes may be reasonably suspected with fasting blood glucose < 100 mg/dL (< 5.6 mmol/L);
— An OGTT should be performed without prior limitations of carbohydrate intake in a fasting, rested subject after an overnight sleep; the subject should remain resting at the site of testing for the 2-hour period before ingestion of 75 g glucose solution and blood sampling, with all blood glucose level measurements performed in venous blood plasma in a laboratory;
— If OGTT is to be performed in a subject with prediabetes treated with metformin for that reason, the drug should be withdrawn at least one week before OGGT;
— OGTT is the preferred method to diagnose IGT. Glucose meter measurements should not be used for diagnostic purposes.

Currently, PTD does not recommend measuring haemoglobin A_{1c} (HbA_{1c}) level to diagnose diabetes.

III. Nomenclature of hyperglycemic states according to the World Health Organization (WHO):

— Normal fasting blood glucose: 70–99 mg/dL (3.9––5.5 mmol/L);
— Impaired fasting glucose (IFG): 100–125 mg/dL (5.6–6.9 mmol/L);
— Impaired glucose tolerance (IGT): 120-minute blood glucose at 120 minutes of OGTT 140–199 mg/dL (7.8–11 mmol/L);
— Prediabetes: IFG and/or IGT;
— Diabetes — one of the following criteria:
1. Symptoms of hyperglycemia and random blood glucose level ≥ 200 mg/dL (≥ 11.1 mmol/L);
2. Fasting blood glucose ≥ 126 mg/dL (≥ 7.0 mmol/L) on two occasions;
3. Blood glucose at 120 minutes of OGTT ≥ 200 mg/dL (≥ 11.1 mmol/L).

IV. Subjects at risk require screening for diabetes, as symptoms of hyperglycemia are absent in more than half of them. Testing for diabetes should be performed every three years in all subjects > 45 years of age. In addition, the following risk groups

Table 1.1. Diagnostic criteria for dysglycemia

Random blood glucose — measured in a blood sample collected at any time of the day, regardless of the timing of the last meal	Fasting blood glucose — measured in a blood sample collected 8–14 hours after the last meal	Blood glucose at 120 minutes during an oral glucose tolerance test (OGTT) according to WHO
	Venous plasma glucose level	
≥ 200 mg/dL (≥ 11.1 mmol/L) → diabetes* (if symptoms of hyperglycemia are present, such as increased thirst, polyuria, fatigue)	70–99 mg/dL (3.9–5.5 mmol/L) → normal glucose tolerance (NGT)	< 140 mg/dL (7.8 mmol/L) → normal glucose tolerance (NGT)
	100–125 mg/dL (5.6–6.9 mmol/L) → impaired fasting glucose (IFG)	140–199 mg/dL (7.8–11.0 mmol/L) → impaired glucose tolerance (IGT)
	≥ 126 mg/dL (≥ 7.0 mmol/L) → diabetes*	≥ 200 mg/dL (≥ 11.1 mmol/L) → diabetes*

WHO — World Health Organization

*Diagnosis of diabetes requires one abnormal reading except for fasting blood glucose which requires two abnormal readings. A potential effect of factors not related to testing itself should be taken into account when measuring blood glucose (timing of the last meal, exercise, time of the day)

should be tested annually regardless of age:

— Overweight or obese subjects [body mass index (BMI) ≥ 25 kg/m^2 and/or waist circumference > 80 cm (women) or > 94 cm (men)];
— Subjects with a family history of diabetes (in parents or siblings);
— Physically inactive subjects;
— Members of community or ethnic groups characterized by increased rates of diabetes;
— Those with prediabetes identified during previous testing;
— Women with a history of gestational diabetes;
— Women who gave birth to an infant with a birth weight > 4 kg;
— Subjects with hypertension (≥ 140/90 mm Hg);
— Subjects with dyslipidemia [high-density lipoprotein (HDL) cholesterol < 40 mg/dL (< 1.0 mmol/L) and/or triglycerides > 150 mg/dL (> 1.7 mmol/L)];
— Women with polycystic ovary syndrome;
— Subjects with cardiovascular disease.

V. Etiologic classification of diabetes according to WHO:

1. Diabetes type 1
— Autoimmune;
— Idiopathic.
2. Diabetes type 2
3. Other specific forms of diabetes
— Genetic defects of beta cell function;
— Genetic defects of insulin function;
— Exocrine pancreatic diseases;
— Endocrinopathies;
— Drugs and chemicals;
— Infections;
— Rare immunologic forms of diabetes;
— Other genetic syndromes associated with diabetes.
4. Gestational diabetes

Latent autoimmune diabetes in adults (LADA)

The category of autoimmune diabetes type 1 includes slowly progressing diabetes caused by autoaggression. Latent autoimmune diabetes in adults (LADA) is a late manifesting autoimmune form of diabetes in adults, most commonly diagnosed in patients above 35 years of age, characterized by clinical insulin independence in the first months after the diagnosis, with the presence of serum antibodies against glutamic acid decarboxylase (anti-GAD65) and/or other anti-islet antibodies and a low serum peptide C level. LADA is a form of diabetes type 1 with slowly progressive autoimmune-mediated destruction of beta cells. This diabetes subtype is present in 5–10% of subjects with diabetes diagnosed after 35 years of age and categorized as diabetes type 2. Clinical manifestations of LADA do not always allow a definite diagnosis, presenting diagnostic challenges when differentiating with diabetes type 2.

A definite diagnosis of LADA requires identification of autoantibodies typical for diabetes type 1, mostly anti-GAD65, and/or a low serum peptide C level.

Monogenic diabetes

Monogenic diabetes amounts to 1–2% of all diabetes cases. It is caused by single gene mutations. Most forms are associated with a defect of insulin secretion, and the most common ones are maturity-onset diabetes of the young (MODY), mitochondrial diabetes, and neonatal diabetes. Taking into account the monogenic forms in the differential diagnosis of diabetes may contribute to treatment optimization and proper evaluation of prognosis in the patient and his family members. A definite diagnosis of monogenic diabetes is a result of genetic testing. Patient selection for genetic testing for monogenic diabetes and any therapeutic decisions resulting from such a diagnosis should be made in centers with a large experience in this area.

Neonatal diabetes is defined as the disease onset before 9 months of age. Genetic testing should be performed in all patients with persistent neonatal diabetes. This should include testing for mutations in the KCNJ11 gene which codes for Kir6.2 protein. Mutations in this gene are the most common cause of persistent neonatal diabetes. Regardless of age, most patients with KCNJ11 gene mutations may be treated with sulphonylureas which are effective and safe in this group and thus may be used as an alternative to insulin. Further targets for genetic testing include mutation in the insulin genes, the ABCC8 gene coding for SUR1 protein, ad the glucokinase gene. If a mutation in the ABCC8 gene is identified, sulphonylurea treatment may be attempted. Carriers of mutations in the insulin gene and a double mutation in the glucokinase gene need to be treated with insulin. Decisions regarding search for mutations in other genes should be made individually by diabetes specialists (diabetologists) with an appropriate experience in the genetics of diabetes.

In families with an autosomal dominant early-onset diabetes caused by impaired insulin secretion, in most cases without obesity, the differential diagnosis should include MODY and mutations in the responsible genes should be searched for. The most common form of MODY is associated with HNF1A and glucokinase gene mutations.

Typical clinical presentation of MODY due to a HNF1A gene mutation includes:

1. Early onset of diabetes (typically before 25 years of age);
2. No insulin dependence and ketoacidosis, low insulin requirement, detectable peptide C levels despite the disease being present for several years or even longer;

3. Family history of diabetes over at least 2 generations, with an early-onset diabetes in at least two family members. OGTT performed at an early stage of diabetes usually shows high postprandial glucose level elevation with often normal fasting blood glucose;
4. Absence of autoantibodies typical for diabetes type 1;
5. Glycosuria higher than expected based on blood glucose levels.

Chronic complications of diabetes develop in a large proportion of patients with MODY due to a HNF1A gene mutation, and thus optimal disease control should be actively pursued early after the disease onset. Sulphonylureas are the drugs of choice (except for pregnancy or the presence of typical contraindications to these drugs). If these are not effective, combined therapy with insulin, metformin or dipeptidyl peptidase-4 (DPP-4) inhibitors, or insulin monotherapy should be considered.

Testing for glucokinase gene mutations is indicated in the following situations:

1. Persistently elevated fasting blood glucose in the range of 99–144 mg/dL (5.5–8.0 mmol/L);
2. An increase in blood glucose during OGTT lower than 83 mg/dL (4.6 mmol/L);
3. A family history of diabetes in one of the parents, but negative family history does not exclude this form of diabetes.

Healthy nutrition with elimination of simple sugars is the treatment of choice in glucokinase defects due to a single gene mutation; drugs are usually ineffective. HbA_{1c} value characteristic for glucokinase defect is not higher than 7.5%.

Decisions regarding testing for mutations in other genes associated with MODY should be made individually in centers experienced in such testing.

The most common cause of mitochondrial diabetes is the A3243G mutation of the gene coding for leucine tRNA. Testing for this mutation should be performed in case of maternal transmission of an early-onset diabetes associated with deafness in some family members. The therapeutic approach in mitochondrial diabetes may include diet and treatment with sulphonylureas or insulin depending on the degree of defective insulin secretion. Metformin use should be avoided in mitochondrial diabetes.

Cystic fibrosis-related diabetes (CFRD)

Diabetes is present in about 20% of adolescents and 40––50% adults with cystic fibrosis, Diabetes associated with cystic fibrosis is classified as other specific type of diabetes associated with exocrine pancreatic disease, characterized by a slow progression and usually remains asymptomatic for many years. Diabetic ketoacidosis occurs rarely, most likely due to preserved endogenous insulin secretion or concomitant impairment of glucagon secretion. Initially, hyperglycemia is usually seen in circumstances that exacerbate insulin resistance, such as acute and chronic infections, glucocorticoid therapy, and ingestion of large amounts of carbohydrates (intake by oral or intravenous route, gastric tube or percutaneous gastrostomy).

Insulin therapy is the treatment of choice.

Routine annual testing for diabetes should be performed in generally healthy subjects with cystic fibrosis aged ≥ 10 years.

2. Preventing and delaying development of diabetes

Diabetes type 1

Currently, no effective and clinically useful methods exist to prevent diabetes type 1 both in the general populations and in subjects at risk.

Diabetes type 2

Screening should be undertaken with fasting blood glucose measurements or OGTT using 75 g of glucose (see Chapter 1). It is also possible to use HbA_{1c} level measurements to screen for dysglycemia.

I. Risk factors for diabetes type 2 (see Chapter 1).

II. Overview of recommendations regarding prevention and delaying development of diabetes:

— Subjects at a high risk of developing diabetes type 2 should receive appropriate education regarding healthy lifestyle (health benefits related to moderate weight reduction and regular physical activity);
— Indications for screening (see Chapter 1);
— Patients with prediabetes (IFG or IGT) should be advised to reduce weight and increase physical activity. Pharmacological prevention of diabetes by using metformin should be considered in subjects at a high risk of developing diabetes type 2, particularly if IFG or IGT is present;
— Repeated advice regarding lifestyle changes is of paramount importance for the effectiveness of prevention;
— It is recommended to monitor patients for other cardiovascular disease risk factors (e.g., tobacco smoking, hypertension, dyslipidemia) and their treatment;
— Use of diabetogenic drugs should be avoided.

3. Blood glucose monitoring

Current monitoring and retrospective evaluation of blood glucose levels are integral parts of adequate diabetes treatment. Appropriate blood glucose self-monitoring (BGSM) requires regular patient education in this regard, including evaluation of the ability to use glucose meter and interpret BGSM results, i.e. using them for day-to-day modification of nutrition, exercise, and medication doses. Regular HbA_{1c} level measurements are another necessary component of diabetes treatment monitoring.

I. Blood glucose self-monitoring

Blood glucose self-monitoring is an integral part of diabetes treatment.

Patients treated with multiple daily insulin injections or continuous subcutaneous insulin infusion (CSII) should perform a daily blood glucose profile that includes readings at morning fast, before and 60–120 minutes after each main meal, and before bedtime. Frequency and timing of additional measurements should be set individually.

Use of blood glucose monitoring systems including continuous glucose monitoring (CGM) and flash glucose monitoring (FGM) to supplement blood glucose self-monitoring is particularly indicated in patients with labile diabetes type 1 with frequent hypoglycemia episodes and hypoglycemia unawareness, as it improves treatment safety and effectiveness.

Blood glucose self-monitoring is also indicated to reach therapeutic targets in patients treated with single insulin injections, oral antidiabetic agents, diet, and prescribed physical exercise (Table 3.1).

Proper BGSM requires patient education regarding glucose meter use, interpretation of readings, and further management steps. For BGSM, it is recommended to use glucose meters that display plasma glucose level with the declared margin of error of up to 15% for glucose levels ≥ 100 mg/dL (5.6 mmol/L) and 15 mg/dL (0.8 mmol/l) for glucose levels < 100 mg/dL (5.6 mmol/L). Analysis of glucose readings using a computer software may be useful in patients performing ≥ 4 measurements daily. Glucose meters and the technique of their use by the patients should be checked in case of suspected measurement errors and at least once a year at the facility where the patient receives outpatient treatment.

II. Hemoglobin A_{1c} (HbA_{1c})

Hemoglobin A_{1c} level reflects average blood glucose levels during the period of approximately 3 last months, with about 50% of HbA_{1c} currently present in blood being formed during the last month before the measurement.

Hemoglobin A_{1c} level measurements should be performed annually in patients with stable disease in whom the therapeutic targets have been met. In those in whom the therapeutic targets have not been met or the treatment has been modified, HbA_{1c} level should be measured at least every 3 months.

Hemoglobin A_{1c} level measurements should be performed using analytic methods certified by the National Glycohemoglobin Standardization Program (NGSP) (http://www.ngsp.org). Point-of-care testing for HbA_{1c} is also possible when using methods and analyzers certified by NGSP.

It has been suggested that diagnostic laboratories report HbA_{1c} levels in SI units (mmol/mol) in addition to traditional units.

When interpreting HbA_{1c} levels, interfering factors should be taken into account, such as changes in the erythrocyte survival time, hemoglobinopathies, and chemical hemoglobin modifications which may render use of these measurements difficult or impossible.

Table 3.1. Recommended frequency of blood glucose self-monitoring

Treatment regimen	Frequency of blood glucose self-monitoring
Multiple (i.e., at least 3 times daily) insulin injections Intensive insulin therapy, regardless of the diabetes type	Multiple (i.e., at least 4 times daily) readings during the day according to the treatment regimen and patient needs
Diet treatment only	4-point blood glucose profile (fasting and 2 hours post main meals) once a month, once a week at various times of the day
Oral hypoglycemic drugs and/or GLP analogs	4-point blood glucose profile (fasting and 2 hours post main meals) once a week, once daily at various times of the day
Diabetes type 2 treated with fixed insulin doses	1–2 readings daily plus 4-point blood glucose profile (fasting and 2 hours post main meals) once a week plus 7-point blood glucose profile once a month
All patients	Additional immediate readings in case of feeling unwell, sudden illness etc.

GLP — glucagon-like peptide

4. Setting therapeutic targets in diabetes

Most important recommendations

- In diabetic patients, the overall goal of diabetes control is HbA_{1c} level ≤ 7.0% (53 mmol/mol). [**A**]
- In all patients with diabetes type 1 and increased urinary albumin secretion and/or renal dysfunction, a statin is recommended to reduce LDL-C level by at least 50% regardless of the baseline LDL-C level. [**C**]
- In patients with diabetes type 2 and cardiovascular disease or chronic kidney disease, and those > 40 years of age without overt cardiovascular disease but with ≥ 1 risk factor or target organ damage, lipid-lowering therapy is recommended to reach the goal LDL-C level of < 70 mg/dL (1.8 mmol/L). [**B**]
- In patients with diabetes type 2 without target organ damage and risk factors, the goal LDL-C level is < 100 mg/dL (2.6 mmol/L). [**B**]
- The recommended blood pressure goal is < 140/90 mm Hg. [**A**]

I. General considerations

1. Therapeutic targets in diabetes include target blood glucose levels, blood pressure values, lipid profile, and body weight.
2. In older patients and those with comorbidities, who are expected to survive for less than 10 years, therapeutic targets should be relaxed so as to not compromise patient's quality of life.
3. Generally, therapeutic targets and treatment intensification should be largely individualized. In all diabetic patients, and particularly those with diabetes type 2, the following factors should be taken into account when setting therapeutic targets: patient's attitude towards treatment and the expected engagement in the treatment process (including that of patient's family members, caretakers etc.), the risk of hypoglycemia and its possible consequences (more severe in the elderly, and in those with preexisting cardiovascular or nervous system damage), duration of diabetes, expected survival, presence of major vascular diabetic complications and significant comorbidities, the degree of patient's education, and the risk-to-benefit ratio associated with specific therapeutic targets. In some circumstances (e.g., in those with advanced complications and in the elderly), the therapeutic targets should be attained gradually, within several (2 to 6) months.

II. Criteria of adequate blood glucose control (taking into account the above considerations)

A general target:

HbA_{1c} ≤ 7% (≤ 53 mmol/mol)

Individual targets:

a) HbA_{1c} ≤ 6.5% (≤ 48 mmol/mol)
   — Diabetes type 1 [fasting and preprandial blood glucose, including BGSM: 80–110 mg/dL (4.4––6.1 mmol/L); 2-hour post-prandial BGSM < 140 mg/dL (7.8 mmol/L)];
   — Diabetes type 2 of a short duration;
   — In children and adolescents, regardless of the diabetes type. When evaluating blood glucose profile in relation to target HbA_{1c}, values given in Table 4.1 should be consulted, showing mean daily blood glucose values and blood glucose ranges corresponding to specific HbA_{1c} levels.

b) HbA_{1c} ≤ 8.0% (≤ 64 mmol/mol)
   — In patients at an advanced age and/or in diabetics with macroangiopathic complications

Table 4.1. Relation between HbA_{1c} levels and average plasma glucose levels

HbA_{1c}	Average plasma glucose levels		Average fasting blood glucose	Average preprandial blood glucose	Average postprandial blood glucose
	[mg/dL]	[mmol/L]	[mg/dL]	[mg/dL]	[mg/dL]
6	126	7.0			
< 6.5			122	118	144
6.5–6.99			142	139	164
7	154	8.6			
7.0–7.49			152	152	176
7.5–7.99			167	155	189
8	183	10.2			
8–8.5			178	179	206
9	212	11.8			
10	240	13.4			
11	269	14.9			
12	298	16.5			

Correlation between HbA_{1c} and average plasma glucose levels 0.92 (according to *Diabetes Care* 2015; 28: 35)

(previous myocardial infarction and/or stroke) and/or multiple comorbidities;

c) HbA_{1c} level < 6.5% (48 mmol/mol) in women with prepregnancy diabetes contemplating pregnancy, < 6.0 % (42 mmol/mol) in the second and third trimester, if it is not associated with an increased rate of hypoglycemia.

If a diabetic patient aged > 65 years is expected to survive for more than 10 years, gradual attainment of general therapeutic targets should be aimed for, with target HbA_{1c} level ≤ 7%.

Correlation between HbA_{1c} and average plasma glucose levels 0.92 (according to *Diabetes Care* 2015; 28: 35)

III. Criteria of adequate lipid profile control:

— LDL-C level < 70 mg/dL (1.9 mmol/L) or reduction by at least 50% if baseline LDL-C level is 70–135 mg/dL (1.9–3.5 mmol/L) in diabetic subjects at very high cardiovascular risk;

— LDL-C level < 100 mg/dL (2.6 mmol/L) or reduction by at least 50% if baseline LDL-C level is 100–200 mg/dL (2.6–5.2 mmol/L) in diabetic subjects at high cardiovascular risk;

— LDL-C level < 115 mg/dl (3.0 mmol/L) in subjects at low or moderate cardiovascular risk (subjects < 40 years of age with diabetes type 1 but without chronic complications and other cardiovascular risk factors);

— Non-HDL cholesterol level < 100 mg/dL (2.6 mmol/L) in diabetic subjects at very high cardiovascular risk;

— Non-HDL cholesterol level < 130 mg/dL (3.4 mmol/L) in diabetic subjects at high cardiovascular risk;

— Non-HDL cholesterol level < 145 mg/dL (3.7 mmol/L) in subjects < 40 years of age with diabetes type 1 but without vascular complications or other cardiovascular risk factors;

— Triglyceride level < 150 mg/dL (< 1.7 mmol/L);

— HDL cholesterol > 40 mg/dL (> 1.0 mmol/L) [in women, higher by 10 mg/dL (0.275 mmol/L)].

IV. Criteria of adequate blood pressure control:

— Systolic blood pressure < 140 mm Hg;

— Diastolic blood pressure < 90 mm Hg.

Details — see Chapter 12.

5. Organization of care for adult patients with diabetes

Comprehensive diabetes care requires input of adequately competent physicians, nurses or educators engaged in diabetic education, and dietitians. Care should be patient-centered, taking into account individual patient situation, needs, and preferences. Due to multidisciplinary nature of late diabetic complications and concomitant conditions, cooperation with other specialists is also necessary.

Children and adolescents and pregnant women — see relevant chapters.

I. Outpatient care

Modern diabetes treatment requires competencies regarding treatment, monitoring, and patient education to convey appropriate knowledge and motivation to comply with treatment recommendations. Cooperation between primary care physicians and specialists is also required.

II. Goals of primary care

1. Promoting healthy lifestyle to prevent development of dysglycemia.
2. Identification of risk factors for diabetes.
3. Investigating diabetes and prediabetes.
4. Evaluation of the risk of long-term complications.
5. Investigating early stages of long-term complications.
6. Managing patients with diabetes type 2 treated with lifestyle changes (diet, physical activity), and oral agents.
7. Initiation and continuation of insulin therapy combined with oral agents in patients with diabetes type 2.
8. Referring treated patients (at least once a year) for specialist consultations to:
   — Evaluate metabolic control;
   — Evaluate the severity of long-term complications and initiate specific treatment if needed;
   — Provide education regarding lifestyle changes;
   — Set therapeutic targets and treatment plans.

III. Goals of specialist care (Table 5.1)

1. Evaluation of treatment effects and setting therapeutic targets during annual specialist check-ups in diabetic patients managed by primary care physicians.
2. Managing patients with diabetes type 1 and other types of diabetes treated with injected agents [insulin, glucagon-like peptide 1 (GLP-1) receptor agonists].
3. Performing specialist investigations and the differential diagnosis of diabetes types, including diagnosis and treatment of monogenic diabetes and diabetes combined with other diseases.
4. Investigating, monitoring, and preventing progression of long-term complications.
5. Diabetes education.
6. Investigating and managing diabetes in pregnant women (in collaboration with obstetricians).
7. Managing patients with clinically overt complications.
8. Investigating concomitant conditions.

Table 5.1. Recommendations regarding monitoring in adult diabetic patients

Parameter	Comments
Nutritional and therapeutic education	At each visit
HbA_{1c}	Once a year, more frequently if doubts regarding maintenance of normoglycemia or need to verify treatment effectiveness following its modifications
Serum total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides	Once a year, more frequently if dyslipidemia
Albuminuria	Once a year in patients not receiving an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker
Urinalysis (with urine sediment)	Once a year
Serum creatinine + estimation of eGFR	Once a year (beginning at 5 years after the diagnosis in diabetes type 1)
Serum creatinine, Na^+, K^+, Ca^{2+}, PO_4^{3-}	Every six months in patients with elevated serum creatinine
Fundoscopy (with mydriasis)	At 5 years after the diagnosis in diabetes type 1, at the time of the diagnosis in diabetes type 2 (details see Chapter 19)

eGFR — estimated glomerular filtration rate; HbA_{1c} — hemoglobin A_{1c}; HDL — high-density lipoprotein; LDL — low-density lipoprotein

IV. Goals of specialist inpatient care

1. Cases of newly detected diabetes type 1 and diabetes type 2 with symptomatic hyperglycemia.
2. Acute diabetic complications (hypo- and hyperglycemia, diabetic ketosis and coma).
3. Exacerbation of chronic complications.
4. Performance of minor procedures.
5. Modifications of the treatment regimen in patients in whom therapeutic targets cannot be met during outpatient therapy.
6. Initiation of intensive insulin therapy using a personal insulin pump and/or continuous glucose monitoring system (cgms).
7. Initiation of insulin therapy in gestational diabetes and preexisting diabetes previously not treated with insulin.
8. Difficulties with obtaining normoglycemia in pregnant patients with preexisting diabetes.

V. Organizational requirements

Specialist diabetes hospital units

A. Physician personnel — two full-time diabetologists (in pediatric units, two diabetologists or pediatric endocrinologists and diabetologists), alternatively, in addition to a diabetologist, an internist (pediatrician in pediatric units) or endocrinologist with an experience in diabetology confirmed by the diabetes voivodship consultant.

B. Nursing staff — two nurses with an experience in education, with duties limited to education and care for diabetic patients, a diabetes educator if possible.

C. Dietician — with duties limited to diabetes care (at least half-time).

D. Access to specialist consultations (as in diabetes clinics, including psychologist consultations).

Recommended therapeutic team staffing for every 15–20 adult diabetes beds: 2–3 physicians, 2 nurses experienced in care for diabetic patients, a dietician, a psychologist (employed or available as a consultant), and a social worker.

E. Equipment:

— At least one intensive metabolic care bed per 10 regular diabetes beds;

— Space and necessary teaching equipment for education (education room);

— Required equipment: medical scales, blood pressure monitors, intravenous infusion pumps, glucose meters, food scales, neurological hammers, 128 Hz tuning forks, monofilaments, and continuous access to cardiac [exercise testing, electrocardiography (ECG), ECG Holter monitoring, ambulatory blood pressure monitoring, coronary angiography] and vascular (Doppler ultrasonography) investigations.

— Recommended (optional) equipment: continuous subcutaneous glucose monitoring system, ophthalmoscope, pedobarography, neurothesiometer, Doppler cine-loop.

Specialist diabetes clinics

A. Physician personnel — a diabetologist (in pediatric diabetology clinic, a diabetologist or pediatric endocrinologist and diabetologist) and another physician: an internist, pediatrician, or endocrinologist with an experience in diabetology confirmed by the diabetes voivodship consultant.

B. Nursing staff — a nurse with at least one year professional experience in diabetes nursing, with formal duties limited to care for diabetic patients, a diabetes educator if possible.

C. Dietician — with duties limited to diabetes care (at least half-time).

D. Psychologist — employed or available as a consultant.

E. Access to specialist consultations, including services of a(n):
- — Ophthalmologist;
- — Nephrologist;
- — Neurologist;
- — Vascular surgeon or angiology specialist;
- — Cardiologist;
- — Orthopedic surgeon.

F. Social worker

A therapeutic team that includes one physician, one nurse experienced in diabetic nursing, one dietician (part-time) and a psychologist may provide care to 800 adult diabetic patients.

Children and adolescents, pregnant women — see relevant chapters.

G. Equipment in specialist diabetes clinics:
- — Required: medical scales, blood pressure monitors, glucose meters, 128 Hz tuning forks, monofilaments, food scales;
- — Recommended (optional): continuous subcutaneous glucose monitoring system, ambulatory blood pressure monitoring system, ophthalmoscope, neurothesiometer, computers with printers to retrieve and print glucose meter, personal insulin pump, and continuous glucose monitoring system data. However, computer equipment that allows data retrieval from insulin pumps and continuous glucose monitoring systems is necessary for the proper management of patients with diabetes type 1 treated with a personal insulin pump.

VI. Organization of care for patients with diabetic foot syndrome

A. Referral diabetes foot outpatients clinics

1. **Personnel requirements:**
   Physicians: equivalent of at least 2 full-time positions — diabetes specialist with at least one year of documented experience in the management of patients with diabetic foot syndrome;
   Nurses: equivalent of at least 2 full-time positions — at least one year of documented experience in the management and care of patients with diabetic foot syndrome or chronic wounds.
2. An established organizational pathway allowing patient hospitalizations in a unit within the same facility (medical center) that has a contract for diabetology or internal medicine services signed with the Polish National Health Fund (NFZ, Narodowy Fundusz Zdrowia).
3. Access to multidisciplinary care, including surgeon, vascular surgeon, or angiology specialist consultations.
4. Ability to provide intravenous antibiotic therapy.
5. Access to basic imaging modalities, e.g. X-ray, ultrasound (including Doppler studies) and CT and/or MRI.
6. Access to laboratory and microbiologic testing performed in a medical diagnostic laboratory listed in the register of the National Chamber of Laboratory Diagnosticians (KRDL, Krajowa Rada Diagnostów Laboratoryjnych).

B. Basic care outpatients clinics

1. The responsibility of these clinics should include the diagnosis and management of diabetes foot syndrome along with prevention of ulcerations, infections, and Charcot neuro-osteoarthropathy complicating diabetes foot syndrome. These clinics should cooperate with referral clinics where more severe cases are consulted and offered further treatment.

6. Behavioral therapy (lifestyle changes)

Most important recommendations

- All diabetic patients should be offered education regarding the general principles of proper diabetes nutrition by appropriately trained personnel (physician, dietician, diabetes nurse, diabetes educator) and using various methods and techniques, including telemedicine. Detailed nutritional recommendations should be tailored to the needs and capabilities of the patient. [**A**]
- The major macronutrient determining periprandial insulin requirement are carbohydrates. Instruction how to estimate carbohydrate content of a meal to optimize insulin dosing should be a key component of dietary education in patients with diabetes type 1. [**A**]
- There is no single universal diet that would be appropriate for all diabetic patients. The optimal proportions of macronutrients for a given patient should be determined individually, taking into account patient's age, physical activity, presence of diabetes complications, and concomitant conditions. [**E**]
- Due to its pleotropic benefits, physical exercise is an integral part of proper comprehensive diabetes management. For optimal effects, exercise should be regular, undertaken at least every 2–3 days but preferably daily. [**A**]

Behavioral therapy is an indispensable element of all patients of all ages diagnosed with diabetes treatment (both type 1 and type 2). Proper nutrition and physical activity are important in improving the overall patients' health and in the prevention and treatment of chronic complications of diabetes. All patients should be educated on the general principles of proper nutrition in diabetes by authorized persons (doctor, dietician, diabetes nurse , diabetes educator) by using different methods and techniques, including telemedicine. Patient management should include therapeutic lifestyle changes encompassing balanced diet, regular physical activity, avoidance of tobacco smoking and alcohol use, optimal sleep duration, and avoidance of stress. Education for therapeutic lifestyle, adapted to the needs and possibilities of the patient, allows to achieve intended therapeutic target and reduces the costs related to the treatment caused by diabetic complications.

Dietary recommendations

I. General recommendations

The goals of dietary treatment in diabetic patients are to obtain and to maintain:

— Normal (near normal) blood glucose level to prevent diabetic complications;
— Optimal serum lipid and lipoprotein levels;
— Optimal blood pressure values to reduce the risk of vascular disease; and
— Desired body weight.

Dietary treatment includes advice on:

— Individually determined energy value of the diet;
— Calorie distribution over individual meals during the day;
— Food sources that will provide necessary calories, vitamins, minerals, and phytochemicals.
— Products that should be limited.

When planning diet, individual patient nutritional and cultural preferences, age, gender, the level of physical activity, and the economic status should be taken into account.

Nutritional strategy in diabetic patients should include:

— Evaluation of usual dietary intake;
— Nutritional diagnosis;
— Determination of the goal and plan of the dietary intervention;
— Nutritional intervention (individual or group counseling);
— Monitoring of nutrition and evaluation of its effects;
— Correction of the dietary plan if the therapeutic goal has not been reached.

Diabetic patients should be encouraged to adhere to the recommendations on healthy nutrition addressed to healthy subjects, and additionally to:

— Controlling the size of usually consumed portions;
— Monitor carbohydrate intake overall and in individual meals;
— Limit intake of foods containing simple absorbable carbohydrates, including added sugar;
— Consume frequent, regular meals.

There is no single universal diet that would be appropriate for all diabetic patients.

Patients with diabetes type 1 without overweight and obesity should avoid consuming easily absorbable simple carbohydrates and adhere to an appropriately balanced diet. In all cases, the dietary plan and insulin regimen should be individually tailored. Insulin therapy should be adjusted to the patient's dietary habits, meal composition (carbohydrate, protein, and fat content), lifestyle, and physical activity. When planning diet, a priority should be given to estimation of absorbable carbohydrate content of the meal, e.g. using the carbohydrate exchange system. Glycemic index and glycemic load values may also be useful when making dietary choices.

In diabetic patients in the oldest age groups, dietary education should be particularly careful and individualized to provide appropriate protein intake.

Although carbohydrates are the major macronutrient determining periprandial insulin requirement, patients with diabetes type 1 should also be educated regarding the glycemic effect of protein and fat.

In diabetes type 2, the major goals are not only to maintain good metabolic control of the disease but also reduce excess body weight and maintain the desired body weight. Thus, in addition to the above recommendations, a factor of major importance is the total calorie content of the diet which should be adjusted to the patient's age, actual body weight, and the level of physical activity, allowing gradual but systematic body weight reduction. A reduction in the total calorie intake (by 500–1000 kcal/day) should allow gradual but systematic body weight reduction (by about 0.5–1 kg/week).

Body weight reduction may be achieved by using a low-calorie diet with various proportions of macronutrients (protein, fat, carbohydrates). Depending on individual patient preferences, the following diets may be recommended for the prevention and treatment of diabetes: a Mediterranean-type diet, the Dietary Approaches to Stop Hypertension (DASH), portfolio, vegetarian or vegan, low-fat or low-carbohydrate diet. Fasting to reduce body weight is not recommended. Despite various views on the ideal macronutrient proportions, a low-carbohydrate diet remains the gold standard in the management of diabetes in patients who require body weight reduction. Body weight reduction may be achieved by using both a reduced carbohydrate diet and a low-fat diet.

II. Specific recommendations

Diet composition

1. Carbohydrates:
   - No sufficient scientific evidence is available to determine single optimal carbohydrate content in the diet of diabetic patients;
   - Carbohydrates should provide about 45% of the total calorie intake; and if they are consumed in the form of low glycemic index and high fiber content products, their share in the total calorie intake may be even higher (up to 60%). High caloric intake from carbohydrates should also be a feature of the diet in subjects who are very active physically. In contrast, a lower carbohydrate share in the total calorie intake (25–45%) may be temporarily recommended in patients with little physical activity if it cannot be significantly increased, e.g., due to concomitant conditions;
   - The main source of carbohydrates should be whole grain cereal products, especially with low glycemic index (< 55 IG);
   - The major limitation should apply to the intake of simple carbohydrates which should be reduced to the minimum;
   - Artificial sweeteners may be used in doses recommended by the manufacturers;
   - Daily fructose intake should not exceed 50 g. Fructose use as a replacement for sugar is not recommended;
   - Due to a beneficial effect of dietary fiber on postprandial glycemia, dietary fiber content should be about 25–50 g/day or 15–25 g/1000 kcal. Intake of soluble fibers (pectins, beta-glucans) is particularly recommended.
2. Fats:
   - Fats should provide 30–35% of the total calorie intake in the most patients;
   - Saturated fats should provide less than 10% of the total calorie intake, and less than 7% of the total calorie intake in patients with serum LDL cholesterol level ≥ 100 mg/dL (≥ 2.6 mmol/L);
   - Monounsaturated fats should provide 10–15% of the total calorie intake;
   - Polyunsaturated should provide about 6–10% of the total calorie intake;
   - Cholesterol intake should be limited to ≤ 300 mg/day, and < 200 mg/dL in patients with serum LDL cholesterol level ≥ 100 mg/dL (≥ 2.6 mmol/L);
   - To reduce serum LDL cholesterol level, low glycemic index carbohydrates and/or monounsaturated fats should be substituted for saturated fats. It may be beneficial to supplement diet with functional foods containing plant sterols/stanols;
   - Intake of trans fatty acids should be limited to the minimum.
3. Proteins:
   - In most diabetic patients, similarly to the general population, proteins should provide 15–20% of the total calorie intake (about 1–1.5 g/kg body weight/day). In patients with diabetes type 2 and excessive body weight, a low-calorie diet may contain 20–30% of protein. In patients with chronic kidney disease, protein intake should be about 0.8–1 g/kg body weight/day;
   - There is no need to limit animal protein intake, although substituting plant protein (e.g., soy protein) for animal protein may be beneficial in some patients.
4. Vitamins and microelements:
   - Vitamin or microelement supplementation is not recommended unless their deficiencies have been identified;
   - The exceptions are vitamin D3 (supplementation according to the recommendations for the general population) and folic acid (supplementation at the dose of 400 μg in pregnant women).
5. Alcohol:
   - Alcohol intake is not recommended in diabetic patients;
   - Patients should be informed that alcohol inhibits hepatic glucose release and thus its intake (particularly without food) may predispose to hypoglycemia;
   - Acceptable levels of alcohol intake are ≤ 20 g/day of ethanol in women and ≤ 30 g/day in men.

   Alcohol should not be consumed by patients with dyslipidemia (hypertriglyceridemia), neuropathy, or a history or pancreatitis.
6. Salt:
   - Salt intake from all sources should not exceed 5 g per day;
   - If reasonable, patients with hypertension may be advised more strict salt intake limitations according to the DASH diet principles.

Dietary recommendations for special patient populations (e.g., pregnant women, children and adolescents, patients with established nephropathy etc.) are provided in the relevant chapters.

Physical exercise

Due to its pleotropic benefits, physical exercise is an integral part of comprehensive diabetes management. Physical exercise has a beneficial effect on insulin sensitivity, blood glucose control, and lipid profile, promotes body weight reduction, and exerts a beneficial effect on mood, even with subjects with depression.

I. General recommendations regarding physical exercise:

— Initially, moderate physical activity should be recommended, depending on the patient's ability to exercise;
— For optimal effects, exercise should be regular, undertaken at least every 2–3 days, preferably daily;
— Intensive physical activity should be preceded by a 5- to 10-minute warm-up and concluded with cool-down exercises;
— Physical exercise may increase the risk of acute or delayed hypoglycemia;
— Alcohol may increase the risk of hypoglycemia after exercise;
— Dehydration should be prevented when exercising in high ambient temperatures;
— The risk of foot damage during exercise (particularly with coexisting peripheral neuropathy and a reduced pain perception) and the need for appropriate foot care and comfortable shoes should be taken into account.

II. Exercise intensity is determined by the physician based on the full clinical picture

The most appropriate form of exercise in patients with diabetes type 2 aged > 65 years and/or overweight is brisk walking (until panting) 3–5 times a week (approx. 150 minutes/week).

Nordic walking is an appropriate form of exercise in overweight/obese subjects at any age.

Those without significant contraindications, especially in the younger age groups, should be encouraged to increased physical activity , including sports. Such patients require additional education in the effect of glycemic induced by different types of physical activity (e.g. aerobic exercise, effort resistance, interval).

III. Risks of physical exercise in diabetic patients

1. Hypoglycemia:
   — Blood glucose level should be measured before, during, and after exercise;
   — Before planned exercise, reduction of rapid/short-acting insulin dose by 30–50% (depending on individual response) should be considered if peak action of the drug would coincide with the exercise or occur shortly afterwards;
   — During treatment with insulin pump, it is recommended to reduce basal insulin rate by 20–80%, depending on the intensity and duration of exercise, preferably 2 hours before exercise;
   — Before unplanned exercise, an additional portion of simple carbohydrates should be consumed (20–30 g per 10 minutes of exercise), and a reduction of post-exercise insulin dose should be considered;
   — Insulin injections into the limbs about to exercise should be avoided if exercise commences within 30–60 minutes after the injection.
2. Metabolic decompensation:
   — Very intensive, short-lasting exercise (> 90% V_{O2max}) and exercise in hypoxic conditions (e.g., high-altitude climbing) may lead to hypoglycemia and acidosis;
   — If blood glucose level exceeds 250 mg/dL (13.9 mmol/L), urine testing for ketone bodies is indicated in patients with diabetes type 1, and exercise should be avoided if ketonuria is found;
   — Patients with diabetes type 2 should consider a similar limitation if blood glucose level exceeds 300 mg/dL (16.7 mmol/L);
3. In some circumstances, strenuous exercise may have a negative effect on the general health status of the patient:
   — Diabetic proliferative retinopathy — risk of vitreous body bleeding and retinal detachment;
   — Diabetic nephropathy — increase in albuminuria/proteinuria;
   — Autonomic neuropathy — risk of orthostatic hypotension;
   — Risk of myocardial ischemia.

Tobacco control

1. In all current or former smokers, determine:
   — Age at which the patient began smoking;
   — Duration of smoking;
   — Number of cigarettes smoked;
   — Any attempts to quit smoking and duration of abstinence;
   — Duration of current abstinence.
2. Counselling:
   — Explanation of the risks associated with smoking to non-smokers;
   — Advice to quit smoking;
   — Patient support in the decision to quit smoking;
   — Psychological and pharmacological support if needed;
   — Discussion regarding smoking during **each** visit;
   — If the patient refuses to quit smoking, this should be documented in the medical records.

7. Psychological management in diabetes

Most important recommendations

- The mental condition of the patient should be evaluated at the initiation of diabetes treatment and during each subsequent visit. [**B**]
- Depression often coexists with diabetes and significantly increases the risk of diabetes complications. [**B**]
- Diabetic patients should be evaluated for anxiety symptoms, addictions, eating disorders, and cognitive dysfunction. These conditions may significantly impair their adaptation to the disease. [**B**]

The mental state of the patient affects nearly all aspects of the management. Non-compliance to treatment is commonly associated with psychological problems which require identification and appropriate psychotherapeutic interventions. For this reason, education limited to providing the patient with information regarding prescribed therapy and other therapeutic recommendations is not very effective. The mental state of the patient should be evaluated at the treatment initiation and during every visit. Use of appropriate questionnaires and tests is recommended.

1. Psychological support should include:
   — Adequate communication with the patient;
   — Continuous evaluation (monitoring) of the mental state and compliance to treatment, along with psychological interventions.
2. The goals of individualized approach to the patient include:
   — Consideration of the patient's psychosocial status and planning treatment which in the patient's opinion may be realistically undertaken in his or her life situation (which is of major importance for setting the therapeutic plan that will be both optimal and realistic);
   — Developing motivation to engage in optimal management;
   — Avoidance of frightening the patient with adverse consequences of non-compliance to therapeutic recommendations which is ineffective and harmful in most cases;
   — Implementation of effective education based on the psychological diagnosis.
3. Evaluation of the psychological/mental state (psychological diagnosis) in diabetic patients includes the following aspects:
   I. Social and psychological situation.
   II. Patient's quality of life.
   III. Attitudes, beliefs, concerns, and duties related to diabetes (unjustified worries and concerns may reduce the ability to cope with the disease). Ask the following question:
   To what degree do you worry about the future and the possibility that severe complications will develop: (0) It is not an issue at all; (1) It is a minor issue; (2) It is a moderately important issue; (3) It is quite an important issue; (4) It is a very important issue. A score of 3 or more indicates a high risk of developing psychosocial problems.
   IV. Sense of control over the disease. Lacking sense of control over the disease results in choosing approaches to cope with the disease-related stress that are characterized by avoidance of thoughts about the disease and/or reducing emotions provoked by the disease.
   V. Evaluation of the ability to cope with the disease (a trend to reduce search for the optimal coping strategy and focus on solving disease-related problems is seen).
   VI. Evaluation of depressive symptoms (depression often coexists and increases the risk of diabetic complications).

A. Use tools available freely online to screen for depression: the Well-being index WHO-5, www.who-5.org (score < 13 indicates the need to investigate for depression, and score ≤ 7 indicates a high risk of depression) or the Patient Health Questionnaire PHQ-9, www.phqscreeeners.com/overview/aspx (score < 5 is normal, 5–9 indicates mild depression, 10–14 indicates moderate depression, 15–19 indicates moderately severe depression, and 20–27 indicates severe depression).
   OR
B. Ask two questions:
   Did you often feel depressed or hopeless during the last month?
   Did you often lack an interest in undertaking various activities or a feeling of pleasure during these activities?
   A positive answer to one of these questions has a **sensitivity of 97%** and a **specificity of 67%** for the diagnosis of depression. In these circumstances, the patient should be referred to a psychiatrist.

   VII. Evaluation of anxiety symptoms, addictions, eating disorders, reduced cognition (these may significantly impair adaptation to diabetes).

4. Psychological interventions in diabetic patients include:
   — Developing the sense of control over the disease by:

- Providing the patient with comprehensible information regarding the disease and its treatment,
- Collaborative development of therapeutic goals and plans which are realistic from the patient's perspective,
- Gradual achievement of therapeutic goals (small steps strategy),
- Offering help in case of treatment failures (so the patient knows that the physician will help him determine the cause of failure without any negative attitude);

— Developing and maintaining diabetes coping skills focused on solving disease-related problems.

5. Clinically severe depression (depressive episode, dysthymia) and other mental health problems require psychiatric consultation. In case of maladaptation to the disease, psychotherapeutic intervention may be undertaken by a primary care physician or a specialist. Help of a clinical psychologist is necessary in more complex cases.
6. Teamwork

Cooperation of the whole therapeutic team is an important prerequisite of treatment success. Effective communication between team members is required. In diabetes clinics, a psychologist is a necessary member of the specialist therapeutic team.

8. Education

I. Education is targeted at subjects at an increased risk of diabetes, subjects with prediabetes, and those treated for diabetes, and their carers and family members. Education is a constant, integral, and necessary component of diabetes management during each visit. In addition, it should be undertaken in a structured way, including education at the time of treatment initiation, followed be reinforcements based on regular evaluation of the patient's educational needs or if requested by the patient.

1. The educational program should be developed in cooperation with the patient and the treating physician and be closely associated and coordinated with the recommended treatment approach. The patient is an active member of the therapeutic team.
2. The goal of patient education is to support self-management and lifestyle modifications based on the recommended diet and physical activity. Management of obesity is a particularly important issue in diabetes type 2.

II. Effectiveness of self-management programs has been documented. They actively engage participants in the learning process, adjusting the content and form to the individual situation and personal experiences of the participants, and motivate them to set personal behavioral treatment targets, developed in cooperation with the physician.

1. Strategies to integrate diabetes self-management with everyday life activities are recommended. Their goals are to increase patients' empowerment by discovering and using their natural and acquired abilities to take responsibility for their own life.
2. It is recommended to provide individualized education along with group educational programs. Education should be provided by an appropriately trained personnel (physicians, diabetes educators, nurses, dieticians). Other members of the therapeutic team, representing various medical professions, should also participate in education. Both educational programs for subjects with newly diagnosed diabetes and reinforcement programs for patients with long-standing diabetes are needed. It is necessary to offer education to patients' family members and caretakers of children and elderly with diabetes.
3. Modern technologies (DVD, Internet) should be used for educational purposes.
4. Education should focus on setting individual diabetes management goals, taking into account problems specific for a given person. The educational program should include developing skills to influence the course of the disease, as the knowledge itself is not sufficient for optimal diabetes management.
5. Diabetes education in children and adolescents should be tailored to their intellectual capabilities, age, and needs.

III. Framework educational program should include the following components:

1. Support regarding disease acceptance, increasing appropriate motivation for treatment, and increasing patient empowerment.
2. Setting and evaluating individual therapeutic goals based on the disease course, prognosis, recommended treatment, and personal situation of the patient.
3. Basic information about the disease and its treatment (causes, clinical characteristics, course and prognosis, etc.)
4. Teaching the techniques of systematic self-monitoring of blood glucose, ketone bodies, blood pressure etc., and how to manage situations when an intervention is necessary.
5. Teaching the techniques of insulin administration (factors affecting the rate of insulin absorption, sites of insulin administration, appropriate needle length, prevention of insulin-induced lipodystrophy).

6. For patients treated with a personal insulin pump: advantages and disadvantages of and indications and contraindications to insulin pump therapy, principles of programming and modifying basal infusion rate, temporary changes of the basal infusion rate, use of single, delayed, and combination boluses, use of a bolus calculator, setting an infusion system (how to choose the injection site), use of CGM and proper interpretation of glucose level readings, what to do in case of an insulin pump failure — return to treatment using insulin pens, management of initial symptoms of ketoacidosis, principles of withholding insulin infusion in special situations (e.g., sport), technical aspects of insulin pump use, calculation of carbohydrate and protein-fat exchanges, achieving appropriately balanced meal composition, maintaining an electronic self-control diary.
7. Information about the appropriate use of independent and integrated insulin pump intergrated with continuous glucose monitoring (CGM) system — the backward and in real time, about their functions, setting alarms for hypo- and hyperglycemia, dynamics of trend changes, and interpretation of CGM results for the current therapy.
8. Information about diagnosing and treating complications, both acute (hypoglycemia, infections, myocardial infarction, stroke, etc.) and chronic (nephropathy, retinopathy, neuropathy, erectile dysfunction, diabetic foot), along with their risk factors (hyperlipidemia, hypertension, smoking, etc.) and approaches to prevent complications and diseases related to diabetes.
9. Information about healthy nutrition and its role in the management (including practical information about carbohydrate content in foods and creating a nutritional plan based on individual habits, needs, and therapeutic strategies, etc.).
10. Information about the effect of physical exercise on the regulation of blood glucose (hypo- and hyperglycemia, etc.).
11. Information about managing special situations (travel, contraception, pregnancy).
12. Information about social rights of diabetic patients (work, driving license, insurance, etc.).
13. Principles of healthcare utilization (visit frequency, follow-up evaluations), optimal compliance to treatment recommendations.
14. Discussion of the importance of psychological problems in the management of diabetes and opportunities for specialist care.

IV. Duration of the initial education should be at least 5 hours in diabetic patients treated with diet or diet and oral antidiabetic agents, about 9 hours in patients treated with insulin, and 9–15 hours in patients treated with a personal insulin pump, depending on the settings of care (outpatient or inpatients), patient situation, and facility resources. Diabetes education should be initiated in each patient as early as possible after the diagnosis is made and continued during further follow-up, for a total of 5–9 hours in patients with diabetes type 1 and at least 7–14 hours in patients with diabetes type 2. During subsequent years, duration of education must depend on the knowledge already absorbed by the patient, number of previous errors, and the type of developing complications and concomitant disorders.

V. It is recommended to introduce new educational programs of proven efficacy, confirmed by study findings.

VI. Education delivered by physicians, nurses, diabetes educators, and dieticians should be undertaken in parallel to drug treatment, taking into the account the above mentioned time constraints, which requires separate funding within specifically defined and contracted services.

VII. Every education program should be based on the principle of professional diabetologist-patient communication. Its goal is to achieve trust, empathy, and motivation for strict compliance with therapeutic recommendations.

VIII. Standard requirements for an education center:

1. Documentation of the educational activities including: framework educational program and training sessions undertaken with each patient, identification of the local education coordinator, and education-related duties of the healthcare personnel and individual patient education charts.
2. Periodic (at least once a year) evaluation of the patient's self-management of diabetes.
3. Providing patients with an opportunity for periodic (at least once a year) evaluation of the quality of education delivered in a given center.
4. Improving skills of the personnel delivering education (participation in education courses, providing up-to-date knowledge).
5. Consideration of patient evaluation of the quality of the education delivered.

9. General principles of the management of diabetes type 1

Most important recommendations

- The recommended treatment approach is intensive insulin therapy using multiple subcutaneous insulin doses or continuous subcutaneous insulin infusion (CSII) using a personal insulin pump. [**A**]
- A key element of therapy for diabetes type 1 is the patient's ability to modify insulin doses based on carbohydrate meal content, baseline blood glucose level, and planned physical activity. Knowledge of the effect of protein and fat on blood glucose level is also important for optimization of insulin dosage. [**E**]
- In patients with diabetes type 1, use of insulin analogs is preferred due to a lower risk of hypoglycemia and better quality of life. [**A**]

Management of diabetes type 1

— Insulin therapy is absolutely required in patients with diabetes type 1. Insulin therapy should be continued even in the remission phase.

— The recommended treatment approach is intensive insulin therapy using multiple subcutaneous insulin doses or CSII using a personal insulin pump. A prerequisite for effective treatment is appropriate education (as outlined in Chapter 8), allowing self-adjustments of insulin doses by the patient based on systematic BGSM using a glucose meter (as outlined in Chapter 3).

— In patients with diabetes type 1, use of insulin analogs is preferred due to a lower risk of hypoglycemia and better quality of life.

— Optimization of insulin dose is important in insulin therapy for diabetes type 1. Long-term use of supraphysiological amounts of insulin without attempts to identify causes of high insulin requirement and treat the underlying problem — except for specific situations (acute illness, medications increasing insulin requirement, stress) — may lead to adverse metabolic consequences including excessive body weight increase.

— A key element of therapy for diabetes type 1 is the patient's ability to modify insulin doses based on meal calorie content (based on calculating carbohydrate and protein-fat exchanges) and planned intensity of physical activity.

— Use of CGM is indicated with recurrent episodes of severe hypoglycemia or large circadian variation of blood glucose levels.

— Systematic physical exercise should be an integral part of the management of diabetes type 1.

Organization of care for patients with diabetes type 1

— Patients with diabetes type 1 should be cared for by a diabetes specialist since the very diagnosis of diabetes type 1 and afterwards. Such a management approach allows continuous collaboration with an education team (as outlined in Chapter 5) and access to necessary consultations.

— New diabetes type 1 cases and difficult-to-treat acute diabetes complications require admission to the hospital at diabetes care unit.

Goals of diabetes type 1 management

The goal of diabetes type 1 management is to achieve good metabolic control with blood glucose levels as close to normal values as possible and $HbA_{1c} \leq 6.5\%$ unless associated with episodes of hypoglycemia or reduced patient quality of life. In other cases, the therapeutic goal should be $HbA_{1c} \leq 7.0\%$.

Only such a management approach may prevent acute and chronic complications and allow patient to engage in normal, active family, professional, and social life.

Early diagnosis of chronic diabetes complications

— Early diagnosis of diabetes complications is possible with screening for nephropathy, retinopathy, and neuropathy. Screening for these complications in patients with diabetes type 1 is outlined in Chapters 18–20.

— In patients with long-lasting diabetes type 1, diabetic macroangiopathy manifesting as ischemic heart disease, cerebrovascular disease, or peripheral arterial disease may develop earlier compared to the general population. Principles of diagnosing and treating ischemic heart disease are discussed in Chapter 16, and management of stroke and acute coronary syndrome is outlined in Chapters 17 and 16.1, respectively.

Diagnosis and management of acute complications

— An adequately educated patient with diabetes type 1 must know how to treat acute mild to moderate hyper- and hypoglycemia and should be able to manage these conditions independently. More severe conditions require medical intervention as outlined in Chapters 14 and 15.

Special situations in subjects with diabetes type 1

— Patients with diabetes type 1 and good metabolic control, treated with intensive insulin therapy, may

be subjected to one-day surgery (minor surgical procedures). Other principles of perioperative management in patients with diabetes type 1 are outlined in Chapter 25.

— Compared to the general population, diabetes type 1 is more commonly accompanied by endocrinopathies, in particular autoimmune disease of the thyroid (Hashimoto disease, Graves disease) and adrenal cortex (Addison disease), celiac disease, vitamin B12 deficiency anemia (Addison-Biermer anemia), and connective tissue disease. These comorbidities may significantly worsen the course of diabetes type 1. Development of diseases that complicate the metabolic derangements of diabetes requires admission to a specialist unit.

— Obesity with concomitant insulin resistance may be present in subjects with diabetes type 1, resulting in an increased insulin requirement and worsened metabolic control. Diagnosis and management require specialist investigations and therapy.

— Eating disorders including bulimia and anorexia are increasingly common in young patients with diabetes type 1. Diagnosis and management of these conditions require specialist psychiatric treatment in close collaboration with a diabetes specialist.

A well-educated patient with diabetes type 1, treated with intensive insulin therapy with good metabolic control, is able to engage in the same physical activity and achieve similar professional goals as non-diabetic subjects of similar age.

10. Oral antidiabetic agents and GLP-1 receptor agonists in the management of diabetes type 2

Most important recommendations

- Metformin should be the first choice drug when initiating drug therapy of diabetes type 2 unless it is contraindicated or poorly tolerated. [**A**]
- If monotherapy using maximum recommended or tolerated doses becomes insufficient to achieve or maintain target HbA_{1c} level, another oral agent, GLP-1 agonist, or basal insulin should be added. This decision should not be postponed by more than 3–6 months. [**A**]
- The choice of further drugs should be individualized, taking into account their effectiveness, side effects, the effect on body weight, risk of hypoglycemia, cost, and patient preferences. [**E**]
- In patients with cardiovascular disease, particularly previous myocardial infarction, drugs with an established beneficial effect on the cardiovascular risk should be considered first. In addition to metformin, such effect was shown for some GLP-1 agonists and one SGLT-2 inhibitor. Lack of drug cost reimbursement may be a barrier for using these drugs in Poland. [**A**]
- Due to progressive nature of diabetes type 2, insulin therapy is indicated in many patients when the treatment is gradually intensified. [**B**]

Lowering hyperglycemia by comprehensive management of diabetes type 2 (in addition to treating hypertension and dyslipidemia, lifestyle changes, antiplatelet treatment etc.) is of key importance for preventing and delaying progression of chronic complications of diabetes (both macro- and microvascular).

I. **Lowering hyperglycemia occurs by correcting both pathogenetic mechanisms of diabetes type 2, i.e. insulin resistance and impaired insulin secretion. Treatment of diabetes type 2 must be gradual and adapted to the progressive nature of the disease. If the therapy used at a given stage is no longer effective, i.e., target HbA_{1c} level cannot be reached, treatment should proceed to the next step after 3–6 months.**

II. **Management of diabetes type 2**

Step 1. Monotherapy:

— Lifestyle modification (body weight reduction, increasing physical activity to 30–45 minutes/day), reduction of meal calorie content in combination with treatment with metformin;

— To minimize the risk of adverse effects of metformin, mostly gastrointestinal complaints, therapy should be started with small doses which are then gradually increased to the maximum tolerated dose;

— If metformin is not tolerated or contraindicated, therapeutic options included sulphonylureas or DPP-4 inhibitors (using drugs that have been approved for monotherapy), sodium-glucose transport protein 2 (SGLT-2) inhibitors, and peroxisome proliferator activated receptor gamma (PPAR-γ) agonists (pioglitazone); in such cases, DPP-4 inhibitors and SGLT-2 inhibitors should be preferred in obese subjects and those at a high risk

Table 10.1. Drug used for the treatment of diabetes type 2 (insulin — see Chapter 11)

	Metformin	Sulphonylureas	Alpha-glucosidase inhibitor	GLP-1 receptor agonists	DPP-4 inhibitors	PPAR-γ agonist	SGLT-2 inhibitors
Effect/mechanism	Decreased hepatic glucose production, increased insulin sensitivity	Increased insulin secretion	Decreased intestinal polysaccharide breakdown	Increased hyperglycemia-mediated insulin secretion, decreased appetite	Increased hyperglycemia-mediated insulin secretion	Increased insulin sensitivity	Induction of glucosuria
Hypoglycemic effect	High	High	Low	High	Medium	High	High
Fasting blood glucose [mg/dL]	↓ 60–70	↓ 60–70	↓ 20–30 (mainly postprandial)	↓ 50	↓ 50	↓ 50	↓ 20–30
Plasma insulin	↓	↑↑	⇔	↑↑	↑	↓	↓
LDL cholesterol	↓	⇔	⇔	↓	↓ or ⇔	⇔	⇔ or ↑
HDL cholesterol	↑	⇔	⇔	↑	↑	↑	↑
Triglycerides	↓	⇔	⇔	↓	⇔	↓	⇔
Body weight	↓ or ⇔	↑	⇔	↓↓	⇔	↑	↓
Risk of hypoglycemia	⇔	↑	⇔	⇔	⇔	⇔	⇔
Adverse effects	Gastrointestinal upset	Hypoglycemia, increase in body weight	Intestinal (diarrhea, flatulence)	Gastrointestinal upset (nausea, vomiting)	No significant	Fluid retention (edema), increase in body weight, increased risk of long bone fractures	Genital fungal infections, increased thirst
Contraindications	Organ failure (heart, brain, liver, kidneys*, respiratory), alcohol abuse	Heart, liver, kidney failure	Gastrointestinal disease	Gastrointestinal neuropathy	Liver failure	Heart or liver failure, bladder cancer	Renal failure

*See Table 18.3; DPP-4 — dipeptidyl peptidase-4; GLP-1 — glucagon-like peptide 1; HbA_{1c} — hemoglobin A_{1c}; HDL — high-density lipoprotein; LDL — low-density lipoprotein; PPAR-γ — peroxisome proliferator activated receptor gamma; SGLT-1 — sodium-glucose transport protein 2

of hypoglycemia, and a PPAR-γ agonist should not be used in patients with heart failure;
— Therapeutic effectiveness of the oral therapy used may be assessed only after several weeks of treatment.

Step 2. Combined oral therapy:
— Option 2a: Lifestyle modification and adding sulphonylurea, incretin-based therapy (DPP-4 inhibitor or GLP-1 receptor agonist), a SGLT-2 inhibitor, or a PPAR-γ agonist to metformin;
— Option 2b: Lifestyle modification and three-drug therapy including metformin (in all cases) and two other agents with different mechanisms of action from the following classes: sulphonylureas, a-glucosidase inhibitors (acarbose), DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, and PPAR-γ agonist.

It also possible to add basal insulin to metformin, i.e. switching from Step 1 directly to Step 3 treatment, bypassing Steps 2a and 2b.

Step 3. Lifestyle modification and simple insulin therapy [mostly with basal insulin (NPH insulin, long-acting insulin analog); various regimens — see Chapter 11], possibly with continuation of metformin therapy, particularly with continuing overweight.

Step 4. Lifestyle modification and complex insulin therapy, possibly with continuation of metformin therapy, particularly with continuing overweight (see Chapter 11).

If lifestyle modification and complex insulin therapy combined with metformin therapy does not allow achieving the desired degree of metabolic control, incretin-based therapy (DPP-4 inhibitor or GLP-1 receptor agonist), a SGLT-2 inhibitor, or a PPAR-γ agonist may be added.

III. Agents used for the treatment of diabetes type 2 are listed in Table 10.1. Their effect on non-glycemic parameters (i.e., cardiovascular risk, body weight, risk of hypoglycemia, lipid parameters, etc.) should be taken into account when selecting and combining drugs, with due attention paid to treatment individualization (see Chapter 4.I.3). Data from large randomized clinical trials indicate a reduction of total and cardiovascular mortality with the use of GLP-1 agonists and SGLT-2 inhibitors.

IV. Practical algorithm of drug treatment for diabetes type 2 is shown in Figure 10.1.

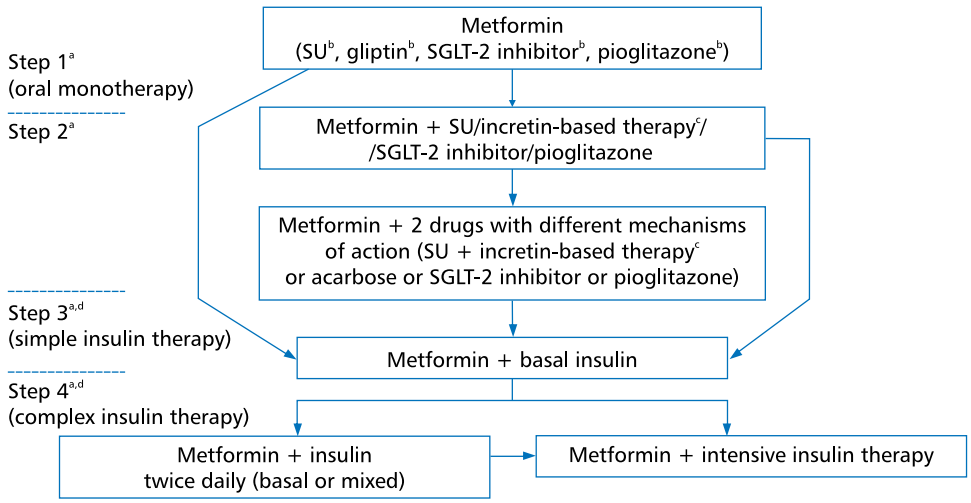

Figure 10.1. A practical management algorithm for diabetes type 2
SU — sulphonylurea; SGLT-2 — sodium-glucose transport protein 2
[a]lifestyle modification recommended at each step
[b]if metformin not tolerated or contraindicated
[c]glucagon-like peptide 1 (GLP-1) receptor agonist or gliptin
[d]in addition to metformin, other oral drugs may also be combined with insulin if licensed for such treatment

11. Insulin therapy

Insulin therapy in patients with diabetes type 1

In patients with diabetes type 1, insulin therapy is the only treatment approach. Intensive insulin therapy with multiple injections or CSII is recommended, using insulin pens or personal insulin pump. In patients with diabetes type 1, insulin analogs are preferred due to a lower risk of hypoglycemia.

Insulin therapy in patients with diabetes type 2

Diabetes type 2 is a progressive disease. Increasing underlying pathophysiologic disturbances, particularly the beta cell defect, result in a need for gradual treatment intensification, including initiation of insulin therapy (see Chapter 10). Insulin therapy is often needed to achieve normoglycemia.

I. Criteria of initiating insulin therapy in diabetes type 2:

— Newly diagnosed diabetes (with an option to return to the typical treatment algorithm):
  • Blood glucose ≥ 300 mg/dL (16.7 mmol/L) with concomitant clinical symptoms of hyperglycemia;
— Treatment ineffectiveness without use of insulin (HbA_{1c} > 7% despite intensified behavioral therapy)

II. Indications for switching from previous glucose-lowering therapy (using oral antidiabetic agents, in some cases in combination with a GLP-1 receptor agonist) to combined therapy including insulin if blood glucose remains uncontrolled:

— Continuing hyperglycemia as confirmed on several occasions;

And

— Unsuccessful attempts to eliminate potentially correctable causes of hyperglycemia, such as:
  • Dietary errors;
  • Too low physical activity;
  • Irregular intake of oral antidiabetic agents (poor compliance);
  • Infections;
  • Inadequate doses of oral agents.

III. Indications for initiating insulin therapy regardless of blood glucose levels:

— Pregnancy;
— Autoimmune-mediated diabetes in adults (type 1/ /LADA);
— Diabetes associated with cystic fibrosis;
— Reasonable patient's request.

In overweight or obese patients with LADA, metformin use combined with insulin therapy is beneficial.

IV. Indications for temporary insulin therapy:

— Diabetes decompensation due to transient causes (infection, trauma, glucocorticoid therapy, etc.);
— Surgical procedure (see Chapter 25);
— Stroke (see Chapter 17);
— Percutaneous coronary intervention (PCI);
— Acute coronary syndrome;
— Other acute illness requiring admission to an intensive care unit.

V. Insulin therapy algorithm

1. Long-acting insulin (isophane — NPH or long-acting insulin analog) in one daily injection:
   — With morning hyperglycemia — in the evening; use of long acting analogues reduces the risk of nocturnal and severe hypoglycemia;
   — With fasting and daytime hyperglycemia — in the morning (consider multiple injections of a short/ /rapid-acting insulin if postprandial hyperglycemia is noticed).

In selected cases, when initiation of insulin therapy was long overdue, resulting in severe hyperglycemia and HbA_{1c} levels much above the therapeutic target, initiation of mixed insulin therapy or intensive insulin therapy should be considered as the initial treatment option, particularly in relatively young patients with long life expectancy. Currently, no convincing evidence exists for better effectiveness or safety of mixed human insulins or insulin analogs. The choice of a particular insulin preparation should be made individually, taking into account patient's preferences regarding the number of daily meals.

2. Initial dose is 0.1–0.2 unit/kg or 10 units.
3. Oral agents and incretin-based therapies may be used according to the registration in subjects treated with insulin:
   — In case of concomitant obesity, combined therapy including insulin and metformin or a-glucosidase inhibitors, or an incretin-based therapy, or a SGLT-2 inhibitor.
   — With normal body weight, combination with a sulphonylurea may be considered.
4. Blood glucose control should be evaluated within 4–5 days, with gradual dose increments by 2–4 units based on SBGM readings until adequate control.
5. If daily basal insulin requirement is > 30 units and glycemia is poorly controlled, treatment intensification may be considered using mixed insulin or biphasic insulin analog; it may also be considered to supple-

ment long-acting insulin (administered once or twice daily) with a short-acting insulin/rapid-acting insulin analog administered at 1–3 meals (basal-plus insulin regimen, intensive insulin therapy). Discontinuation of insulin secretagogues should be considered.

6. If large daily insulin doses are used (> 100 units), indicating insulin resistance, causes of the latter should be considered and the possibility of adverse effects should be taken into account.

An attempt to reduce the degree of insulin resistance by a 72- to 96-hour continuous subcutaneous or intravenous insulin infusion is recommended.

Intensive insulin therapy

Intensive insulin therapy is undertaken based on similar principles in all types of diabetes, using multiple daily insulin injections, or by CSII using a personal insulin pump.

I. Principles of intensive insulin therapy:

— Daily SBGM;
— Self-adjustment of insulin doses or administering additional insulin doses depending on blood glucose readings, energy requirement, and physical activity;
— Precise definition of target blood glucose levels;
— Appropriate therapeutic and nutritional education and patient motivation;
— Possibility of a rapid patient contact with the therapeutic team;
— In diabetes type 2, CSII using a personal insulin pump is not a routine treatment approach.

II. Algorithms of multiple insulin injections:

— Short-acting insulin or rapid-acting insulin analog before meals; and
— Isophane insulin (NPH) or long-acting insulin analog to provide constant basal insulin levels administered before bedtime and/or in the morning.

In some cases of diabetes type 2 with normal fasting blood glucose levels, short-acting insulin injections or insulin analog at mealtimes may be sufficient.

III. Personal insulin pump treatment algorithm

Therapy with personal insulin pumps should be undertaken in centers experienced in such treatment. This approach is used in diabetes type 1 and some other specific diabetes types (e.g. diabetes associated with cystic fibrosis).

1. Indications:
   — Need for small insulin doses (e.g., in children);
   — Recurrent, unpredictable hypoglycemia episodes;
   — Hypoglycemia unawareness;
   — Irregular lifestyle and meals;
   — Early-morning hyperglycemia;
   — Pregestational diabetes mellitus which is difficult to control with multiple insulin injections;
   — Patient preference if costs incurred by this treatment approach are accepted.
2. Contraindications:
   — Low intellectual or educational level of the patient;
   — Lack of patient compliance;
   — No contact with a specialist clinic.

12. Treatment of hypertension in diabetic patients

Most important recommendations

- The aim for blood pressure in patients with diabetes is < 140/90 mm Hg. [**A**]
- The drug of first choice in the treatment of hypertension in patients with diabetes are drugs blocking of the renin–angiotensin–aldosterone system. [**A**]
- Pharmacological treatment of hypertension should be continued without interruption, because it is the only way to reduc cardiovascular risk. [**A**]
- In the treatment of hypertension patients with diabetes should strive not only to achieve the target blood pressure, but also to maintain or restore normal diurnal variation in blood pressure assessed by 24-hour monitoring. [**B**]

In patients with diabetes, initiation of drug treatment is recommended if blood pressure is above 140/90 mm Hg. The goal of treatment is to reduce the global cardiovascular event risk by lowering systolic blood pressure below 140 mm Hg, while the optimal diastolic blood pressure is 90 mm Hg.

I. Principles of blood pressure measurement

Blood pressure should be measured during each visit, also in the standing position to evaluate orthostatic blood pressure falls. Home blood pressure measurements are recommended in all patients with the diagnosis of hypertension. In patients with systolic blood pressure ≥

140 mm Hg or diastolic blood pressure ≥ 90 mm Hg, measurement should be repeated on another day, and out-of-office blood pressure measurements should be recommended. Systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg during repeated measurements confirms the diagnosis of hypertension. In case of diagnostic uncertainties, 24-hour ambulatory blood pressure measurement (including evaluation of night-time blood pressure values) is useful, along with home blood pressure measurements performed by the patient.

II. Principles of antihypertensive therapy:

- Drug treatment should be combined with lifestyle changes in all patients with hypertension;
- Drug treatment should be started with lowest doses available to minimize adverse effects;
- If the target blood pressure has not been reached, the dose of a single drug may be increased to a medium dose; if the treatment is still unsuccessful, a second drug from another class should be added; maximum drug doses should not be used;
- The presence of proteinuria does not change predefined blood pressure goal;
- In stage 2 and 3 hypertension, treatment is initiated with two drugs, with an option to increase the dose of one or two drugs to the maximum dose, particularly if the systolic/diastolic blood pressure exceeds the recommended target value by ≥ 20/10 mm Hg;
- Effective combined therapy should include drugs of different classes with different mechanisms of action to achieve an additive blood pressure-lowering effect; preferred combinations: an angiotensin-converting enzyme inhibitor (ACEI) + calcium antagonist (a metabolically neutral combination); ACEI + thiazide/thiazide-like diuretic, angiotensin receptor blocker (ARB) + thiazide/thiazide-like diuretic, ARB + calcium antagonist (a metabolically neutral combination);
- A combination of an ACEI and a beta-blocker is commonly used in patients with hypertension and cardiac disease (ischemic heart disease, heart failure);
- Combinations of drugs with similar mechanisms of action are of little value, as the blood pressure-lowering effect is less than additive or an increased risk of adverse effects exists;
- If a given drug if not effective or not tolerated by the patient, substitution with a drug from another class is recommended before the dose is increased or another drug is added;
- Use of fixed-dose combinations increases compliance;
- A drug from another class should be added if target blood pressure has not been reached despite two-drug treatment (one of the drugs used should be a diuretic);
- In case of a non-dipping nocturnal blood pressure pattern or a morning blood pressure surge, modification of the timing of antihypertensive drug administration should be considered;
- Long-acting antihypertensive drugs which allow 24-hour blood pressure control with once daily dosing should be preferred;
- Serum creatinine, potassium, and glomerular filtration rate (GFR) should be monitored during treatment with ACEI, ARB, renin inhibitors, and diuretics;
- In patients aged > 65 years, blood pressure should be lowered gradually to avoid treatment complications.

III. Choice of blood-pressure lowering drugs

An effective treatment resulting in normalization of blood pressure is more important for the prevention of cardiovascular complications than the choice of drugs:

- Drug treatment may be initiated with an ACEI, ARB, diuretic, beta-blocker (vasodilating beta-blockers are preferred if no compelling indications are present that would suggest otherwise), or a calcium channel blocker;
- Renin-angiotensin-aldosterone (RAA) system inhibitors should be preferred if albuminuria/proteinuria is present;
- Combined treatment with ACEI and ARB is contraindicated;
- Combined treatment may include drugs from the above listed and other drug classes, taking into account the principles of combining antihypertensive drugs;
- Drug treatment of hypertension in patients with concomitant renal dysfunction — see Chapter 18;
- In patients aged > 55 years with concomitant cardiovascular risk factors, treatment with ACEI should be considered to reduce the cardiovascular risk regardless of blood pressure values;
- ACEI or ARB is recommended in normotensive subjects with urinary albumin-to-creatinine ratio ≥ 30 mg/g to prevent and delay progression of diabetic kidney disease;
- In patients with ischemic heart disease, previous myocardial infarction, or heart failure, beta-blockers and ACEI are reasonable as first-choice drugs to reduce mortality risk;
- Use of nonselective beta-blockers should be avoided with concomitant peripheral arterial disease;
- In case of coexistence of peripheral arterial disease, taking non-selective β-bleckers should be avoided;

— Thiazide/thiazide-like diuretics should be used in patents with GFR ≥ 30 mL/min/1.73 m^2, while a loop diuretic should be used if GFR is < 30 mL/ /min/1.73 m^2.

Clinical studies indicate that use of at least two different antihypertensive drugs is necessary to reach therapeutic goals in more than 70–75% patients, and > 90% of the elderly patients. Often, this requires use of other drug classes in addition to those listed above (including alpha-blockers, centrally-acting drugs, and vasodilators).

Resistant hypertension, which requires multiple drug therapy, is common in diabetes. Testing for obstructive sleep apnea should be considered in diabetic patients with resistant hypertension.

Principles of diabetes management in children and adolescents, pregnant women and those contemplating pregnancy, and patients above 65 years of age — see Chapters on respective subjects.

IV. Management of hypertension in pregnant women

The goal blood pressure is < 140/90 mm Hg but diabetic nephropathy in pregnant women is an absolute indication to lower blood pressure below 130/80 mm Hg.

In pregnant women with non-severe hypertension, oral drugs of choice are (in the order given) methydopa, labetalol, and calcium antagonists. In life-threatening situations, the preferred drugs are labetalol and nitroglycerin (administered parenterally). If these are not available, parenteral hydralazine may be used, although an increase in the rate of adverse effects in the perinatal period has been reported.

13. Treatment of dyslipidemia

Most important recommendations

- In all patients with diabetes type 1 and increased urinary albumin excretion and/or renal dysfunction, statin treatment to reduce LDL-C level by at least 50% is recommended regardless of baseline LDL-C level. [**C**]
- In patients with diabetes type 2 and cardiovascular disease or chronic kidney disease, or patients > 40 years of age without overt cardiovascular disease but with ≥ 1 cardiovascular risk factor or target organ damage, target LDL-C level during treatment is < 70 mg/dL. [**B**]
- In patients with diabetes type 2 without target organ damage and other cardiovascular risk factors, target LDL-C level is < 100 mg/dL. [**B**]

The main goal is to reduce LDL cholesterol level, while non-HDL cholesterol level is a secondary therapeutic target. Complete normalization of the atherogenic lipid profile after achieving target LDL cholesterol level, i.e. increasing HDL cholesterol level and decreasing triglyceride level, may be associated with beneficial effects.

Diabetic patients with vascular complications (previous myocardial infarction, acute coronary syndrome, coronary revascularization or other revascularization procedures, stroke, transient ischemic attack, aortic aneurysm, and peripheral arterial disease) or other cardiovascular risk factors, i.e. albuminuria, hypertension, hypercholesterolemia, smoking, or a family history of cardiovascular disease should be considered at **very high cardiovascular risk**. Patients without chronic diabetes complications and other cardiovascular risk factors are at **high cardiovascular risk**. Only in young patients with diabetes type 1 without chronic diabetes complications and other cardiovascular risk factors, the risk is **moderate or low**.

I. Diagnosis of lipid disorders

History should include:

— Assessment of nutrition and alcohol intake;
— Assessment of physical activity — type and duration of activity;
— Presence of cardiovascular disease: ischemic heart disease, cerebrovascular disease, and peripheral arterial disease;
— Evaluation for thyroid, liver, and kidney disease to exclude secondary hyperlipidemia;
— Family history of lipid disorders, cardiovascular disease, hypertension, and diabetes in first-degree relatives;
— Use of drugs that may increase lipid levels.

Desirable levels of lipid parameters:

— LDL-C level < 70 mg/dL (1.9 mmol/L) or reduction by at least 50% if baseline LDL-C level is 70–135 mg/dL (1.9–3.5 mmol/L) in diabetic subjects at very high cardiovascular risk;
— LDL-C level < 100 mg/dL (2.6 mmol/L) or reduction by at least 50% if baseline LDL-C level is 100–200 mg/dL (2.6–5.2 mmol/L) in diabetic subjects at high cardiovascular risk;
— LDL-C level < 115 mg/dL (3.0 mmol/L) in subjects at low or moderate cardiovascular risk (subjects < 40 years of age with diabetes type 1 but

without chronic complications and other cardiovascular risk factors);
- Non-HDL-C level < 100 mg/dL (2.6 mmol/L) in diabetic subjects at very high cardiovascular risk;
- Non-HDL-C level < 130 mg/dL (3.4 mmol/L) in diabetic subjects at high cardiovascular risk;
- Non-HDL-C level < 145 mg/dL (3.7 mmol/L) in subjects < 40 years of age with diabetes type 1 but without chronic complications and other cardiovascular risk factors;
- HDL-C: no target level but values > 1.0 mmol/L (> 40 mg/dL) in men and > 1.2 mmol/L (> 45 mg/dL) in women indicate a lower risk.

Triglycerides:
- No target level but values < 1.7 mmol/L (< 150 mg/dL) indicate a lower risk.

LDL cholesterol level may be estimated using the Friedewald formula if triglyceride level is < 400 mg/dL (< 4.5 mmol/L) and LDL cholesterol level cannot be directly measured:
- LDL cholesterol [mmol/L] = total cholesterol [mmol/L] – HDL cholesterol [mmol/L] – triglycerides/2.2 [mmol/L]

II. Lipid level monitoring

1. Diabetes type 2
   - Lipid parameters should be measured at the time of the diagnosis of diabetes, with follow-up measurements annually or more frequently, depending on the measured levels;
   - If lipid parameters are above the normal values, these should be re-checked every 8–12 weeks after treatment initiation until the desired levels are reached;
   - If lipid parameters are within the desired range, follow-up measurements should be performed annually;
2. Diabetes type 1 (see also the respective chapter on diabetes type 1):
   - If lipid levels indicate low risk, lipid parameters should be re-checked every 2–5 years, depending on the presence of other risk factors for cardiovascular disease.

III. Treatment of dyslipidemia in diabetic patients

1. Lifestyle changes:
   - Increase in physical activity;
   - Body weight reduction in overweight and obese subjects;
   - Cessation of tobacco smoking;
   - Diet with a reduction of saturated fat intake to < 10% of the total calorie intake, reduced cholesterol (< 300 mg/day or < 200 mg/day with increased LDL cholesterol levels), and maximum reduction of trans fat intake; intake of n-6 polyunsaturated fatty acids should be 4–8% of the total calorie intake, and intake of n-3 polyunsaturated fatty acids should be 2 g of linolenic acid and 200 mg/day of very long-chain fatty acids;
   - In hypertriglyceridemia, reduction of obesity, reduced alcohol intake, reduced mono- and disaccharide intake (reduction of fructose intake), reduced saturated fat intake, adding monounsaturated fats to diet, and reduction of carbohydrate intake are all of major importance.
2. Tight glycemic control

   Tight glycemic control is of major importance for controlling dyslipidemia, in particular hypertriglyceridemia.
3. Drug treatment
   - Statins are first-line drugs in the treatment of diabetic dyslipidemia. They are recommended in all patients with diabetes type 2 or diabetes type 1 at the age of > 40 years. They may also be considered in subjects < 40 years of age if the risk is significantly elevated due to the presence of microvascular complications or other cardiovascular risk factors.

   Drug treatment, mostly with statins, is used in:
   - In diabetic patients with concomitant cardiovascular diseases;
   - In diabetic patients with chronic kidney disease;
   - In diabetic patients > 40 years of age without concomitant cardiovascular disease but with ≥ 1 cardiovascular risk factor or markers of target organ damage.

     Statin therapy should be considered in patients with diabetes type 1 or 2 aged 18–39 years without concomitant cardiovascular disease in whom LDL-C level is > 100 mg/dL (> 2.6 mmol/L) or cardiovascular risk in increased due to the presence of other risk factors (such as diabetic nephropathy, retinopathy, poor glycemic control, hypertension, positive family history of premature vascular disease) or long duration of diabetes.
   - In diabetic patients with concomitant hypertriglyceridemia ≥ 2.3 mmol/L (≥ 200 mg/dL) persisting despite attainment of the target LDL cholesterol level using a statin, an increase in statin dose should be considered to reduce non-HDL cholesterol level which is a secondary therapeutic target. Combination treatment with a fibrate should be considered in selected cases;
   - Statin treatment is contraindicated during pregnancy and breastfeeding.
4. Combined therapy
   - In statin-treated patients with diabetes type 2 in whom triglyceride level is > 2.3 mmol/L (> 200 mg/dL) and HDL cholesterol level is < 0.88 mmol/L (< 34 mg/dL), adding a fibrate to a statin is associated with an additional reduction of cardiovascular events;

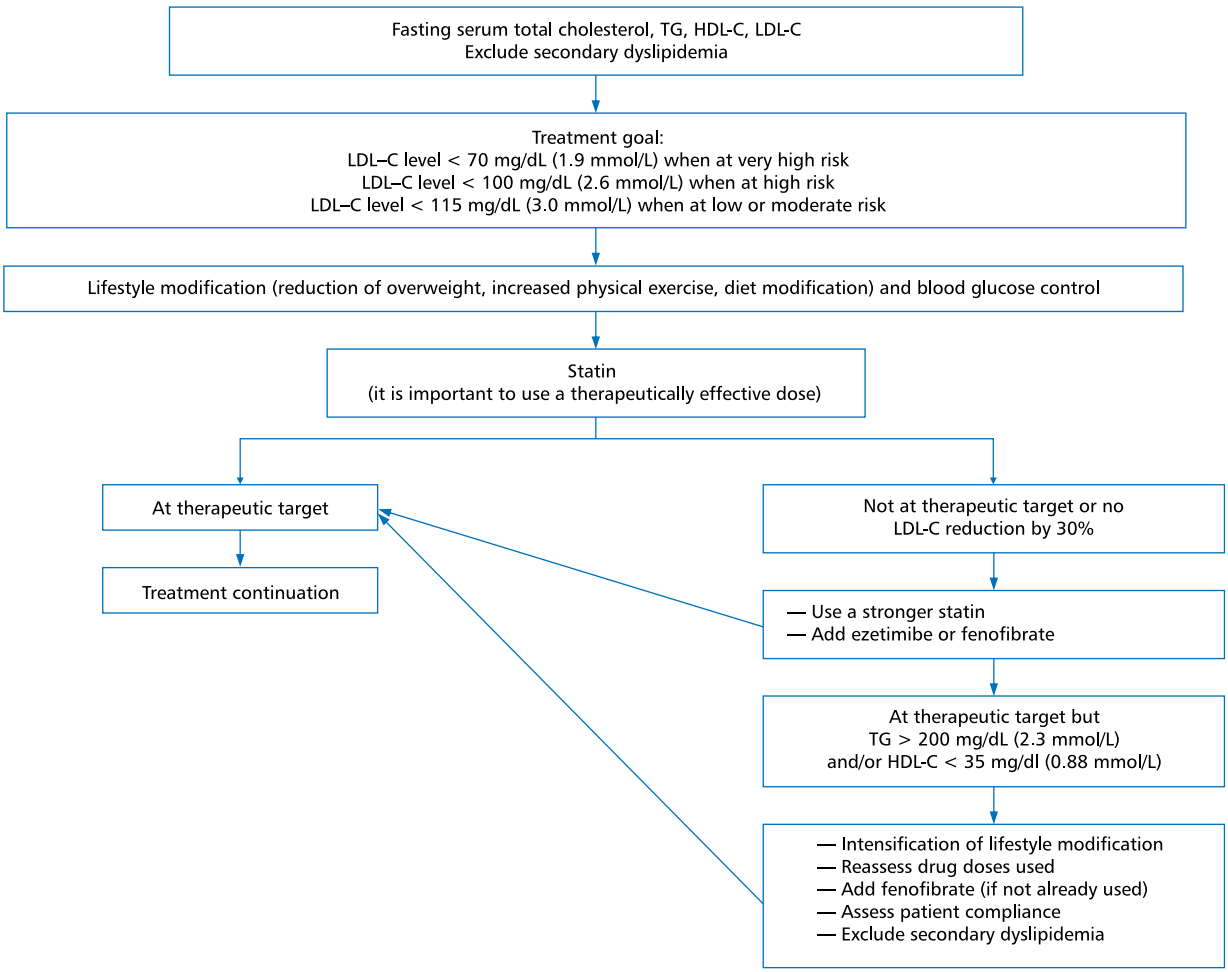

Figure 13.1. An algorithm for managing dyslipidemia in diabetes. TG — triglycerides; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol

Table 13.1. Indications for specific intensities of statin treatment in diabetic patients

Age	Risk factors	Recommended statin dose
< 40 years	No	Not recommended
	IHD risk factors*	Moderate or high
	IHD present**	High
40–75 years	No	Moderate
	IHD risk factors*	High
	IHD present**	High
> 75 years	No	Moderate
	IHD risk factors*	Moderate or high
	IHD present**	High

IHD — ischemic heart disease

*IHD risk factors: low-density lipoprotein cholesterol ≥ 100 mg/dL (2.6 mmol/L), hypertension, smoking, overweight or obesity. **History of a cardiovascular event or current acute coronary syndrome

— Combined statin and ezetimibe treatment was associated with further LDL cholesterol level lowering and a reduction in the cardiovascular event rate compared to statin monotherapy. Ezetimibe may thus be of use in patients in whom recommended LDL cholesterol lowering has not been attained using a maximum tolerated statin dose or statin treatment is not tolerated.

Combined treatment with statins and other lipid-lowering drugs (fibrates, ezetimibe, PCK9 inhibitors) me be useful to achieve target lipid parameters in diabetic patients but no large clinical trials have been conducted to confirm efficacy and safety of such treatment.

Combined therapy (mostly with statin + fenofibrate) is associated with an increased risk of abnormal liver function tests, myositis, and rhabdomyolysis, particularly

with concomitant chronic kidney disease and use of high drug doses.

5. Management of severe hypertriglyceridemia

A clinically significant risk of acute pancreatitis occurs with triglyceride levels > 10 mmol/L (> 880 mg/dL). Hypertriglyceridemia underlies about 10% of acute pancreatitis cases, but pancreatitis may develop already with triglyceride levels > 5 mmol/L (> 440 mg/dL).

Recommended management includes:

— Hospital admission in case of acute pancreatitis;
— Strict control of triglyceride levels:
  • Reduction of the total calorie intake and fat intake (to 10–15% of the total calorie intake),
  • Complete abstinence from alcohol,
  • Therapy with fibrates.

In diabetic patients who are not treated with insulin, insulin therapy should be started to achieve optimal blood glucose control, most commonly using intravenous insulin pump. This approach allows reduction of triglyceride levels within 2–5 days.

Principles of diabetes management in children and adolescents, pregnant women and those contemplating pregnancy, and patients above 65 years of age — see Chapters on respective subjects.

14. Hypoglycemia

I. Definition of hypoglycemia. Hypoglycemia is diagnosed when blood glucose level falls below 70 mg/dL (3.9 mmol/L) regardless of clinical symptoms which may occur only with lower blood glucose levels in some patients, particularly those with long-standing diabetes type 1 present for many years. Symptoms of hypoglycemia may also develop with higher blood glucose levels (> 100 mg/dL) if a rapid decrease in blood glucose has occurred. So called hypoglycemia unawareness, defined as unawareness of pathologically low (< 70 mg/dL, i.e. < 3.9 mmol/L) blood glucose levels, is a significant complication of frequent hypoglycemia episodes. Hypoglycemia unawareness may also be due to autonomic neuropathy.

Blood glucose levels < 70 mg/dL (3.9 mmol/L) require counteracting further blood glucose lowering regardless of the presence or absence of clinical symptoms. This justifies setting the threshold for imminent hypoglycemia at 70 mg/dL.

Severe hypoglycemia is an episode requiring help of another person to administer carbohydrates, glucagon, or initiate other measures. Exact blood glucose values during the episode may be not available but resolution of symptoms following normalization of blood glucose is considered a sufficient proof that the episode was caused by low blood glucose levels.

Recurrent severe hypoglycemia: two or more episodes of severe hypoglycemia during last 12 months.

II. General considerations

1. Diabetic subjects should not be automatically considered at risk of hypoglycemia and thus handicapped in terms of employment and the social status.
2. Risk of hypoglycemia is increased in the following situations:
   — Insulin use as monotherapy or in combination with other antidiabetic agents;
   — Sulphonylurea use as monotherapy or in combination with other antidiabetic agents;
   — Inappropriate dosing of the above mentioned agents in the settings of increased physical activity, reduced calorie intake or alcohol consumption;
   — Aiming for rapid HbA_{1c} level normalization.
3. Hypoglycemia may be directly life-threatening in some situations (the elderly, patients with ischemic heart disease)

III. Management of hypoglycemia unawareness:

— Patient and family member education regarding identification of subtle and atypical prodromes of hypoglycemia;
— Consideration of this problem during professional activities and driving;
— Treatment modifications leading to a significant reduction of hypoglycemia episodes as the only approach to improve hypoglycemia awareness;
— Frequent BGSM, consideration of CGM.

IV. Management of recurrent hypoglycemia episodes includes thorough evaluation of patient's habits and current treatment of diabetes and other conditions, and modification of diabetes therapy to minimize the risk of hypoglycemia (e.g., by reducing insulin dose before anticipated physical exercise, switching to another insulin type, etc.).

V. Acute management of hypoglycemia

1. In a conscious patient:
   — Depending on the degree of hypoglycemia, administer orally 10–20 g of glucose (glucose tablets or gel) or a sweetened beverage;

— A dose of 10–20 g of glucose will raise blood glucose level after about 10–20 minutes. To avoid recurrent hypoglycemia, complex carbohydrates should be consumed and blood glucose level should be re-evaluated after 60 minutes;
— Blood glucose should be monitored;
— Consider subcutaneous or intramuscular glucagon administration, educate patient's relatives how to administer glucagon;

2. In an unconscious patient or a person with impaired consciousness and unable to swallow:
— Intravenous administration of 20% dextrose solution (0.2 g dextrose/kg body weight) followed by infusion of 10% dextrose;
— If intravenous access is difficult, administer 1 mg of glucagon intramuscularly or intravenously (0.5 mg in children < 6 years of age);
— Upon return of consciousness, administer carbohydrates orally until complete resolution of the risk of recurrent hypoglycemia;
— In patients with diabetes treated with insulin or sulphonylureas, prolonged hypoglycemia may occur that sometimes requires prolonged glucose infusion;
— If severe hypoglycemia occurs, hospital admission should be considered due to a life-threatening condition associated with a risk of irreversible lesions in the central nervous system.
3. In patients receiving intensive insulin therapy using insulin analogs or a personal insulin pump, management of hypoglycemia usually includes only administration of 15 g of glucose orally and rechecking blood glucose level after 15 minutes. If blood glucose level continues to be low, glucose should be re-administered and blood glucose level rechecked after further 15 minutes (the 15/15 rule). If oral intake of simple carbohydrates is not possible during personal insulin pump treatment, interruption of basal insulin infusion and repeated blood glucose measurements are indicated.
4. In patients treated with long-acting insulins (human or insulin analogs) a possibility of delayed recurrent hypoglycemia after initial successful treatment should be taken into consideration.

15. Management of acute diabetes complications due to hyperglycemia

I. Classification

1. Diabetic ketoacidosis (mortality: 0.2–2%; mortality risk is increased in patients with recurrent episodes of diabetic ketoacidosis).
2. Hyperglycemic hyperosmolar state (mortality — about 15%).
3. Lactic acidosis (mortality — about 50% according to the historical data but depends to a large degree on the experience of the treating center, the severity of the underlying disease, and concomitant conditions).

II. Ketoacidosis

1. Causes of diabetic ketoacidosis and ketoacidotic coma:
— Interruption or errors of insulin therapy;
— Too late diagnosis of diabetes type 1;
— Alcohol abuse;
— Acute inflammation (e.g., bacterial, viral, and fungal infections);
— Pregnancy;
— Other.
2. Diagnosis:
Laboratory criteria of diabetic ketoacidosis:
— Blood glucose usually > 250 mg/dL (> 13.9 mmol/L), blood glucose values may be lower in patients treated with SGLT-2 inhibitors;
— Blood pH < 7.3;
— Serum bicarbonate level < 15 mmol/L;
— Presence of ketone bodies in urine or serum;
— Anion gap: Na^+ (mmol/L) – [Cl^- (mmol/L) + HCO_3^- (mmol/L)] > 12 (measured and not corrected sodium level is used in this formula).
3. Differential diagnosis:
— Fasting ketosis;
— Alcohol-induced ketoacidosis [blood glucose level rarely > 250 mg/dL (13.9 mmol/L), serum bicarbonate level usually ≥ 18 mmol/L];
— Metabolic acidosis with anion gap > 20 mEq/L (ethylene glycol, methanol, paraldehyde, or salicylate poisoning);
— Lactic acidosis (blood lactate level may also increase in ketoacidosis);
— Other comatose conditions leading to hyperglycemia and ketosis, or the latter accompanied by e.g., stroke or uremic coma.
4. Monitoring of ketoacidosis:
— Evaluation of blood pressure, heart rate, breathing rate, and the degree of consciousness: every 1–2 hours;
— Fluid balance: every 1–2 hours;
— Body temperature measurements: every 8 hours;
— Blood glucose measurements: every hour;
— Serum sodium and potassium measurements: every 4 hours [corrected serum sodium level should be calculated using the formula: measured serum Na^+ + 2.0 mmol/L per each 100 mg/dL (5.6

mmol/L) of blood glucose level above 100 mg/dL (5.6 mmol/L)];
— If serum potassium > 5.5 mmol/L when potassium is not supplemented: serum potassium measurement after 2 hours, and after normalization — every 4 hours;
— Blood gases: every 4 hours;
— Baseline blood and/or urine ketones.

5. Management:

A. Patient hydration:
— Water deficit (on average 100 mL/kg body weight) should be corrected intravenously within 24–48 hours with monitoring of the patient's cardiovascular status:
• 1000 mL 0.9% saline within first hour,
Followed by:
• 500 mL/h 0.9% saline for 4–6 hours,
Followed by:
• 250 mL/h 0.9% saline until normalization of acid-base balance,
• When blood glucose is reduced below 250 mg/dL (13.9 mmol/L), add 5% dextrose infusion at 100 mL/h; if dextrose infusion is added after 24 hours of fluid therapy, decrease the rate of 0.9% saline infusion to 150 mL/h,
• In situations associated with increased energy requirement (e.g., ketoacidosis associated with infection, hyperthyroidism, pregnancy), it is recommended to substitute 10% dextrose for 5% dextrose, administered at the rate of 70 mL/ /hour;

B. Correcting hyperglycemia:
— Intravenous insulin therapy:
• Initial insulin bolus 0.1 unit/kg body weight,
• Followed by intravenous insulin infusion at 0.1 unit/kg body weight/hour with blood glucose monitoring,
• The rate of infusion should be adjusted depending on current blood glucose level, measured every hour,
• Hourly blood glucose level reduction should be not higher than 100 mg/dL (5.6 mmol/L),
• If plasma glucose level does not fall by 50–70 mg/dL (2.8–3.9 mmol/L) from the baseline value during the first hour, increase (usually double) the rate of intravenous insulin infusion until constant blood glucose level reduction by 50––70 mg/dL (2.8–3.9 mmol/L) per hour is reached.

C. Correction of electrolyte disturbances:
— Potassium deficit in a person with ketoacidosis is 3–5 mmol/kg body weight;
— Potassium supplementation according to the following principles:
Serum potassium level:
• K^+ > 5.5 mmol/L → do not administer KCl;
• K^+ 5.0–5.5 mmol/L → 5–10 mmol KCl per hour;
• K^+ 4–5 mmol/L → 10–15 mmol KCl per hour;
• K^+ 3–4 mmol/L → 15–20 mmol KCl per hour;
• K^+ < 3 mmol/L → stop insulin infusion and administer 25 mmol KCl per hour.

Potassium supplementation > 15 mmol/h should be administered via a central venous line or to two peripheral veins.

D. Bicarbonate administration — consider only if arterial blood pH < 6.9 (in small doses, not more than 1 mmol/kg body weight); increased lactate level in ketoacidosis (which is often associated with mild lactate level elevation due to tissue ischemia) is not an indication for bicarbonate administration.

6. Treatment adverse effects:
— Hypokalemia related to insulin administration and correction of acidosis with bicarbonates;
— Hypernatremia, mostly related to inappropriate administration of sodium bicarbonate (np. pulmonary edema, cerebral edema; intravenous mannitol infusion at 1–2 g/kg body weight during 20 minutes is recommended in case of cerebral edema;
— Hyperglycemia caused by interruption of intravenous insulin administration following initial improvement, without early initiation of subcutaneous insulin treatment;
— Hypoglycemia due to overly intensive insulin therapy;
— Hyperchloremia due to administration of excessive amounts of saline.

7. Complication of diabetic ketoacidosis:
— Hypovolemic shock;
— Acute renal failure
— Cerebral edema, more commonly in children.

8. Management of acute ketoacidosis in children — see Figure 22.1.

III. Hyperglycemic hyperosmolar state

1. Causes:
— Most commonly due to a delayed diagnosis or inadequate treatment of diabetes type 2, stroke, or myocardial infarction, following consumption of large amounts of alcohol, use of some diuretics, in patients with chronic kidney disease, mental health problems, and evidence of infection.

2. Diagnosis

Laboratory diagnostic criteria of a hyperglycemic hyperosmolar state:
— Blood glucose > 600 mg/dL (> 33.3 mmol/L);
— pH > 7.30;
— Serum bicarbonate level > 15.0 mmol/L;

— Hypernatremia: corrected serum sodium level (calculated using the formula given above) ≥ 150 mmol/L;
— Serum ketone bodies: absent/trace;
— Effective plasma osmolality > 320 mOsm/kg H_2O.

Effective plasma osmolality (mOsm/kg H_2O) = 2 [Na^+ (mmol/L)] + blood glucose (mmol/L) {2 [measured Na (mEq/L)] + [blood glucose (mg/dL)]/18}

Normal plasma osmolality is 280–300 mOsm/kg H_2O.

3. Differential diagnosis:
— Ketoacidotic coma;
— Comatose states due to central nervous system disease;
— Uremic coma;
— Coma due to poisoning.
4. Management

The approach to management is similar to the management of diabetic ketoacidosis, except for bicarbonate administration:
— Blood glucose lowering (similar insulin doses as in the management of diabetic ketoacidosis);
— Normalization of plasma osmolality (with gradual reduction by no more than 3 mOsm/kg H_2O per hour);
— Subcutaneous administration of a low molecular weight heparin;
— Correction of water and electrolyte deficits:
• Water deficit is much larger than in patients with diabetic ketoacidosis;
— Use of a hypotonic multi-electrolyte solution (0.45% saline or hypotonic multi-electrolyte solution), followed by normal saline when plasma osmolality has been normalized, with monitoring of the patient's cardiovascular status.
• The rate of saline infusion is determined based on serum sodium level and plasma osmolality;
— Blood glucose and electrolyte monitoring.

IV. Lactic acidosis

1. Causes:
— Type A is due to cardiogenic shock, massive bleeding, septic shock, acute or chronic respiratory failure (it is not characteristic for diabetes) but three fourths of diabetic patients die due to cardiovascular causes; this condition may also occur in diabetic patients.
— Type B is due to causes other than hypoxemia. It develops in patients with diabetes, liver disease, malignancies, and following ingestion of ethanol, biguanides, salicylates, and methanol.
2. Laboratory diagnostic criteria:
— Moderately elevated blood glucose (but may also be normal);
— Reduced blood pH (< 7.30), bicarbonate level < 10 mmol/L, anion gap > 16 mmol/L;
— Lactate level > 5 mmol/L;
— Normal serum sodium level (may be reduced in alcohol abuse);
— Usually increased serum potassium level.
3. Management:
— Includes the following measures:
• Preventing and counteracting shock (correction of hypovolemia, vasoconstrictors in moderate doses),
• Counteracting hypoxemia and hypoxia,
• Reducing excessive lactate production (glucose and insulin infusion with blood glucose monitoring),
• Alkalinization by administration of sodium bicarbonate (requirement: base excess × 0.3 × body mass in kg),
• In some cases, renal replacement therapy may be required (biochemical and/or clinical indications).

16. Diagnosis and management of ischemic heart disease in diabetic patients

Ischemic heart disease (IHD) is the major cause of mortality among diabetic patients. Diagnosis and management of IHD and heart failure in this patient population are the same as in subjects without dysglycemia.

I. Differences in the clinical course of IHD in diabetic patients indicate the need for follow-up assessment of risk factors in this population at least once a year.

II. Indications for diagnostic, functional, and anatomic investigations to diagnose IHD and stratify risk in diabetic patients (a cardiology consultation) (Figure 16.1):

1. Presence of typical or atypical cardiovascular symptoms or signs.
2. Abnormal resting ECG.
3. Concomitant atherosclerotic lesions in carotid or peripheral arteries.

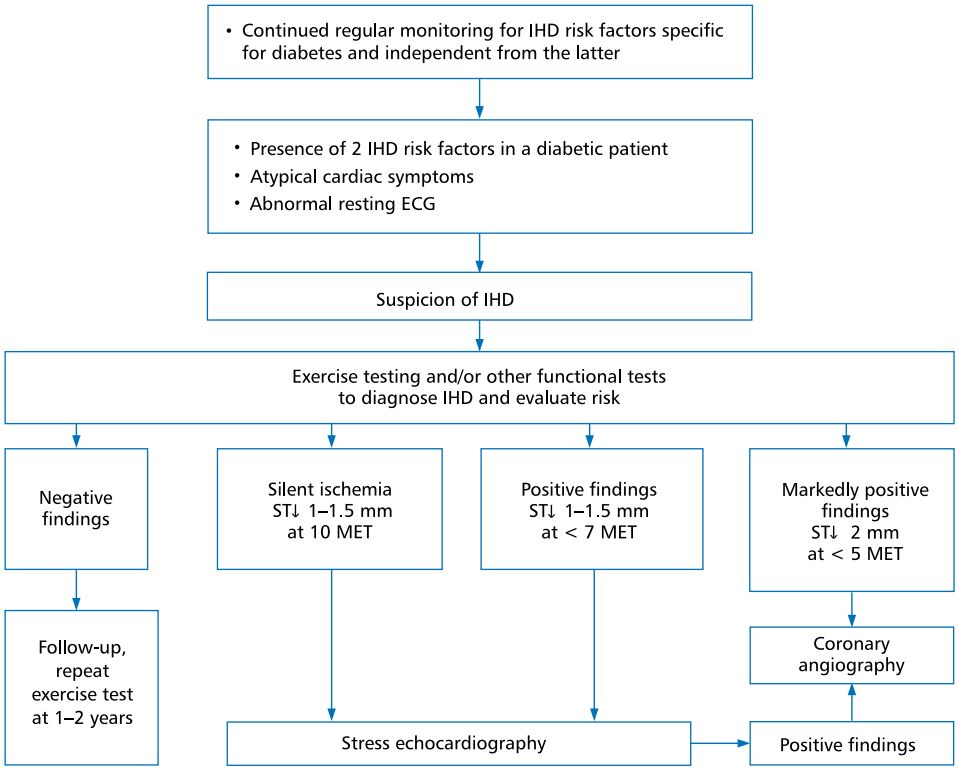

Figure 16.1. An algorithm for the diagnosis of and risk stratification in ischemic heart disease (IHD) in diabetic patients. ECG — electrocardiogram; MET — metabolic equivalent

4. Planned intensive physical exercise in subjects > 35 years of age who previously lived a sedentary lifestyle.
5. Diabetes type 1 for > 15 years.
6. Presence of at least two risk factors for IHD in addition to diabetes:
   — Dyslipidemia (see Chapter 4);
   — Hypertension;
   — Smoking;
   — Family history of premature atherosclerosis;
   — Albuminuria;
   — Autonomic neuropathy.

III. Management of stable IHD in diabetic patients

1. Initiation of a healthy lifestyle (see Chapter 6).
2. Lipid-lowering therapy to achieve therapeutic targets (see Chapter 4).
3. Reduction or elimination of risk factors for IHD:
   — Blood pressure normalization (see Chapter 12);
   — Treatment of dyslipidemia (see Chapter 13).
4. Drug therapy for IHD in diabetes
   Antiplatelet therapy:
   — Acetylsalicylic acid should be also used in patients > 40 years of age with diabetes type 1 or 2 and an increased cardiovascular event risk (IHD risk > 5% during 10 years). Effectiveness of acetylsalicylic acid in the primary prevention in diabetic patients has not been established.
   - The recommended acetylsalicylic acid dose is 75–100 mg/day,
   - If acetylsalicylic acid is contraindicated, clopidogrel 75 mg/day may be beneficial although new antiplatelet agents (i.e., prasugrel and ticagrelor) are currently preferred due to their higher effectiveness; if these are unavailable, clopidogrel is recommended,
   - Dual antiplatelet therapy (acetylsalicylic acid 75–100 mg/day, clopidogrel 75 mg/day) is recommended in patients after a percutaneous coronary intervention (PCI). Duration of dual antiplatelet therapy depends on the presentation of IHD and the type of the implanted stent. Recommended treatment duration is one month after the procedure in stable IHD treated with a bare metal stent (BMS), and 6–12 months after implantation of a drug-eluting stent (DES). In all patients after an acute coronary syndrome, dual antiplatelet therapy for 12 months is recommended;

   — Cardioselective beta-blockers or combined alpha$_1$- and beta-adrenergic blockers:

- RAA system inhibitors;

— Additional therapy:

- Omega-3 fatty acids: a beneficial effect on the development and progression of IHD has been suggested.

If drug treatment is not successful, coronary revascularization should be considered.

Exercise testing and other functional (stress) tests are used to confirm the diagnosis, document ischemia, stratify risk, and guide selection of treatment modalities and evaluate their effectiveness. Exercise ECG is still most easily available and thus most commonly performed but its sensitivity and specificity for diagnosing ischemia is limited, particularly in women. Other functional (stress) tests include stress echocardiography, myocardial perfusion scintigraphy, magnetic resonance imaging (MRI), and positron emission tomography (PET). Among anatomical methods, invasive coronary angiography remains the gold standard, although multidetector computed tomography (MDCT) may also be useful. Diabetic patients are usually at moderate to high coronary artery disease risk. Functional tests are recommended as first-choice modalities in moderate-risk patients, while coronary angiography is the major first-choice modality in high-risk patients. An advantage of MDCT is its high negative predictive value and thus this modality is mostly useful to exclude significant coronary artery disease. However, it s not recommended in high-risk patients, as it results in unnecessary contrast agent and radiation exposure.

16.1. Management of acute coronary syndromes in diabetic patients — glucose-lowering therapy

In acute coronary syndromes, normalization of blood glucose levels using intravenous insulin infusion is recommended in somewhat vague states of relative hyperglycemia, which should be defined as blood glucose level above 140 mg/dL (7.8 mmol/L) in subjects with established diabetes and above 180 mg/dL (10.0 mmol/L) in subjects without a previous diagnosis of diabetes. Intravenous insulin administration is the only approach that allows rapid normalization of blood glucose levels and improvement of outcomes following an acute coronary syndrome. If possible, a diabetologist should be involved in the management of IHD in patients with dysglycemia.

I. The first day of an acute coronary syndrome

1. Stop oral antidiabetic agents.
2. Measure blood glucose on admission in all patients with an acute coronary syndrome.
3. If blood glucose is above 140 mg/dL (7.8 mmol/L) in subjects with established diabetes or above 180 mg/dL (10.0 mmol/L) in subjects without a previous diagnosis of diabetes, initiate intravenous insulin infusion at the rate shown in Table 16.1.1. Recommended frequencies of blood glucose measurements during daytime: every 1 hour, followed by every 2 hours when blood glucose levels become stabilized. Blood glucose level should be kept at 100–180 mg/dL (5.6–10 mmol/L) by adjusting appropriately the rate of insulin infusion.
4. Serum potassium level should be monitored during insulin infusion.

If blood glucose increases above 180 mg/dL (10 mmol/L), temporarily stop intravenous glucose infusion, restarting it when blood glucose falls to 180 mg/dL (10 mmol/L), and at the same time increase the rate of intravenous insulin infusion.

5. If meals are consumed by the patient, add intravenous boluses of a short-acting insulin.
6. If diabetic ketoacidosis is present, treat accordingly (Chapter 15).

II. From the second day of an acute coronary syndrome until discharge

1. Target blood glucose values during glucose-lowering therapy are 100–180 mg/dL (5.6–10.0 mmol/L)

Table 16.1.1. Approximate insulin infusion rate in relation to blood glucose level

Blood glucose	10% dextrose [ml/hour]	Insulin [unit/hour]
<100 mg/dL (< 5.5 mmol/L)	50	Stop infusion for 15–30 minutes
100–140 mg/dL (5.5–7.8 mmol/L)	50	0.5–1.0
140–180 mg/dL (6.7–10.0 mmol/L)	50	1.0–2.0
180–250 mg/dL (10.0–13.9 mmol/L)	Stop infusion until blood glucose < 180 mg/dL (10.0 mmol/L) then 50	2.0–4.0
250–300 mg/dL (13.9–17.4 mmol/L)	Stop infusion until blood glucose < 180 mg/dL (10.0 mmol/L) then 50	4.0–6.0

throughout 24 hours. Thus, treatment must be individualized, preferably in cooperation with a diabetologist.

2. In patients without evidence of acidosis, with dysglycemia diagnosed on the first day of an acute coronary syndrome or with previous successful metformin treatment, appropriate diet may allow adequate metabolic control of diabetes in this period (Chapter 6). In the remaining cases, initiate insulin therapy with multiple injections as described earlier (Chapter 11).
3. In overweight or obese patients with diabetes type 2, metformin may be started before discharge, even as early as on the third day after the coronary intervention, if not contraindicated. A reduction in insulin dose may be possible after 2–3 days of metformin therapy.

III. Following discharge

Metformin should be started in all patients with diabetes type 2 after an acute coronary syndrome, unless contraindicated or not tolerated.

In patients with diabetes type 2 in whom good metabolic control (see II.1 in this chapter) was achieved at the time of discharge and daily insulin requirement does not exceed 30 units, it is possible to return to previous glucose-lowering treatment that was used before the acute coronary syndrome. In overweight or obese patients with diabetes diagnosed during the hospital stay and good metabolic control (see II.1) achieved at the time of discharge, with daily insulin requirement not exceeding 30 units, oral metformin therapy may be used, combined with other agents if needed. If good metabolic control cannot be achieved or daily insulin requirement exceeds 30 units, insulin therapy should be continued. Following an acute coronary syndrome, each patient with dysglycemia should be urgently referred to a diabetologist.

Note 1: In all patients with an acute coronary syndrome, except for those with previously established diabetes, oral glucose tolerance test (see Chapter 1, III, Table 16.1.1.) should be performed before discharge. It glucose intolerance or diabetes is diagnosed, a diabetologist should be consulted.

Note 2: Metformin should be withdrawn at least 48 hours before elective diagnostic or therapeutic cardiac catheterization/coronary angiography. The drug may be resumed 24 hours after coronary angiography.

17. Stroke in diabetic patients

Diabetes is a strong risk factor for stroke, both ischemic and hemorrhagic.

Elevated blood glucose is seen in as many as 60% of patients hospitalized due to an acute stroke. In about 20% of cases, hyperglycemia occurs in subjects with established diabetes, in 16–24% of cases in patients without previous diagnosis of diabetes, and in the remaining cases it is intermittent hyperglycemia (stress hyperglycemia).

Hyperglycemia in the acute phase of stroke is an adverse prognostic factor both in diabetic patients and in those without diabetes. Its presence is associated with a risk of a larger ischemic area and its hemorrhagic transformation, a more severe course of the condition, and a worse prognosis (lower degree of patients' independence and increased early and late mortality). Hyperglycemia found on admission often tends to decrease gradually and spontaneously within first several hours to days after the stroke onset.

Target blood glucose levels in patients with acute stroke are similar to that in other severely ill patients with hyperglycemia. Insulin therapy should be initiated if blood glucose is ≥ 180 mg/dL (10 mmol/L), and blood glucose should be kept at 140–180 mg/dL (7.8–10 mmol/L), preferably close to 140 mg/dL (7.8 mmol/L). Blood glucose levels below 110 mg/dL (6.1 mmol/L) should be avoided to the risk of hypoglycemia.

Insulin should be given intravenously in 0.9% saline using a syringe pump, with strict monitoring of blood glucose levels. The rate of insulin infusion should be modified depending on blood glucose levels measured every 1 hour, and every 2 hours after stable blood glucose values are obtained. A general algorithm for modifying the rate of intravenous insulin infusion depending on blood glucose levels is shown in Table 16.1.1. Serum potassium level should be checked 2–3 times a day during insulin infusion.

It is not recommended to administer insulin as glucose-insulin-potassium (GIK) infusion. Insulin should not be administered subcutaneously during the first two days of stroke or longer in unconscious patients.

Physicians and nursing personnel in the acute stroke care unit should be trained in the treatment of hyperglycemia using a specified intravenous insulin dosing algorithm, with adjustments of the insulin infusion rate in relation to blood glucose levels.

When the patient's condition improves and meals begin to be given orally, intravenous insulin infusion should be stopped and subcutaneous insulin dosing should be initiated. Withdrawal of intravenous insulin should be preceded by subcutaneous administration of a short-acting insulin or rapid-acting insulin analog by about 1 hour before the planned cessation of intravenous insulin infusion. The recommended treatment regimen includes

a short-acting insulin or rapid-acting insulin analog before meals and long-acting insulin once or twice daily. In some cases, it is sufficient to give a short-acting insulin or rapid-acting insulin analog before meals. Insulin should be given before food, with dosing based on blood glucose readings immediately before meals.

Due to a high likelihood of diabetes in patients with an acute stroke and no previous diagnosis of diabetes, investigations for diabetes are needed after the patient's condition has stabilized.

Recommendations regarding management of hypertension and other aspects of care for patients with an ischemic stroke are the same as in non-diabetic patients, as no evidence is available to indicate benefits from any different or specific management of diabetic patients.

Secondary prevention after stroke should be instituted according to the general recommendations in this regard.

18. Prevention, diagnosis, and treatment of diabetic kidney disease

I. In diabetic patients, urinary albumin excretion, serum creatinine, and estimated GFR should be determined to detect and evaluate the severity of diabetic nephropathy. Albuminuria and estimated GFR are independent predictors of cardiovascular and renal risk in diabetic patients.

II. Screening for albuminuria should be performed according to the following principles:

— Testing should be performed annually, beginning at 5 years after the diagnosis of diabetes type 1 and at the time of the diagnosis of diabetes type 2;

— Urinalysis should be performed first to detect/exclude overt proteinuria or a urinary tract infection; if overt proteinuria is found, there is no need to investigate albumin excretion;

To evaluate albuminuria:

— An albumin/creatinine (ACR) ratio should be determined in a single (spot) urine sample (preferably morning urine sample) — for interpretation of the results see Table 18.1; or

— Albumin excretion rate (AER) should be measured in a 24-hour urine collection or a single morning urine collection. Albuminuria determined in a 24-hour urine collection may be considered an equivalent of albuminuria expressed in mg per 1 g of creatinine (i.e., ACR). For interpretation of the results see Table 18.1.

If a positive AER result is obtained, investigations should be repeated twice during 3 months. Albuminuria may be diagnosed based on 2 positive results out of 3 AER measurements. Urinary albumin excretion is increased by physical exertion during preceding 24 hours, infection, hyperglycemia, heart failure, and high blood pressure.

III. Abnormal urinary albumin excretion is defined in Table 18.1.

IV. Serum creatinine level in diabetic patients should be measured at least annually regardless of urinary albumin excretion and used for estimation of GFR.

V. Glomerular filtration rate should be estimated using the following formulas:

MDRD formula

— For serum creatinine (SCr) in mg/dL:

$$\text{Estimated GFR (mL/min/1.73 m}^2) = 186 \times [\text{SCr}]^{-1.154} \times (\text{age})^{-0.203} \times 0.742 \text{ (in women)}$$

$$\text{Estimated GFR (mL/min/1.73 m}^2) = 186 \times [\text{SCr}]^{-1.154} \times (\text{age})^{-0.203} \text{ (in men)}$$

— For serum creatinine (SCr) in μmol/L:

$$\text{Estimated GFR (mL/min/1.73 m}^2) = 186 \times [\text{SCr}/88.4]^{-1.154} \times (\text{age})^{-0.203} \times 0.742 \text{ (in women)}$$

$$\text{Estimated GFR (mL/min/1.73 m}^2) = 186 \times [\text{SCr}/88.4]^{-1.154} \times (\text{age})^{-0.203} \text{ (in men)}$$

or

Table 18.1. Definitions of abnormal urinary albumin excretion*

Category	AER [mg/day]	ACR (spot urine sample) [mg/day or mg/g creatinine]*	Albumin excretion [μg/min] in urine collection
A1 normal to slightly increased albuminuria	< 30	< 30	< 20
A2 moderately increased albuminuria	30–300	30–300	20–200
A3 overt proteinuria	> 300	> 300	≥ 200

AER — albumin excretion rate; ACR — albumin/creatinine ratio

*As the amount of albumin excreted with urine per 1 g of creatinine is approximately equal to 24-hour urinary albumin excretion, this approach allows avoiding errors of 24-hour urine collection

CKD-EPI formula

$$GFR = 141 \times \min(SCr/\kappa, 1)^{\alpha} \times \max(SCr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018 \text{ (for women)}$$

Where

SCr — serum creatinine

κ = 0.7 for women and 0.9 for men

α = –0.329 for women and –0.411 for men

min = the minimum of SCr/κ or 1

max = the maximum of SCr/κ or 1

VI. Stages of chronic kidney disease are defined in Table 18.2.

VII. It is recommended to perform annual evaluation of albuminuria in patients with established increased urinary albumin excretion (if the patient does not receive an optimal therapy with ACEI or ARB).

VIII. If estimated GFR decreases below 60 m mL/min/ /1.73 m^2 or treatment of hypertension becomes difficult, a nephrology consultation should be considered. If estimated GFR decreases below 30 mL/min/1.73 m^2, a nephrology consultation is mandatory.

Nephrological work-up for proteinuria should be considered in patients with short duration of diabetes type 2 and no changes in fundoscopy.

IX. Recommendations for prevention

1. Blood glucose, blood pressure, and lipid control should be optimized to reduce the risk of nephropathy or delay its progression.
2. Tobacco smoking is an independent risk factor for development and progression of nephropathy in patients with diabetes type 2.
3. Yearly screening for albuminuria and determination of serum creatinine level is indicated in patients with diabetes type 1 beginning at 5 years after the diagnosis, and in all patients with diabetes type 2 beginning at the time of the diagnosis.

Table 18.2. Stages of chronic kidney disease

Category	Description	eGFR [mL/ /min/1.73 m^2]
G1	Kidney damage* with normal or high eGFR	≥ 90
G2	Kidney damage* with mildly decreased eGFR	60–89
G3a	Moderately decreased eGFR	45–59
G3b	Moderately to severely decreased eGFR	30–44
G4	Severely decreased eGFR	15–29
G5	End-stage renal failure	< 15

eGFR — estimated glomerular filtration rate

*Kidney damage is defined as urinalysis and/or urine sediment abnormalities and/or abnormalities in blood markers of kidney damage and/or imaging studies of the kidneys or urinary tracts persisting for more than 3 months

X. Management

1. Therapeutic targets for blood glucose, lipid parameters, and blood pressure as described in Chapter 4 should be aimed for to delay progression of diabetic nephropathy.
2. If albuminuria is found, therapy with ACEI or ARB should be initiated (unless contraindicated) as these drugs reduce the risk of progression of nephropathy.
3. In patients with diabetes type 1 with concomitant hypertension and albuminuria, ACEI delay progression of nephropathy at any stage.
4. In patients with diabetes type 2 with concomitant hypertension and albuminuria, both ACEI and ARB delay progression of nephropathy.
5. In patients with diabetes type 2 with concomitant hypertension, albuminuria, and in the category G3a or higher chronic kidney disease (estimated GFR < 60 mL/ /mL/1.73 m^2), ARB delay progression of nephropathy.
6. Serum creatinine and potassium should be monitored during treatment with ACEI, ARB, and/or a diuretic.
7. In albuminuric patients receiving optimal treatment with ACEI or ARB, the importance of annual evaluation of urinary albumin excretion is questionable.
8. Combining ACEI with ARB is not recommended. When evaluating potential benefits of other possible combinations of RAA system inhibitors (e.g., more effective reduction of progression of renal or heart failure), the risk of significant adverse effects should always be considered.
9. Daily dietary protein intake should be reduced to 0.8–1.0 g/kg body weight in patients with diabetes complicated with chronic kidney disease in the category G1–G2. In the category G3–G5 and in patients with overt proteinuria, daily dietary protein intake should be reduced to ≤ 0.8 g/kg body weight (about 10% of the daily calorie intake).
10. In patients in whom therapeutic targets are not met during ACEI or ARB therapy, addition of calcium channel blockers, beta-blockers or diuretics should be considered.
11. Use of a thiazide/thiazide-like diuretic may be considered (thiazide-like diuretics are preferred) with estimated GFR ≥ 30 mL/min/1.73 m^2, while a loop diuretic should be used with estimated GFR < 30 mL/min/1.73 m^2.
12. Use of aldosterone antagonists may decrease the rate of GFR reduction in some patients, provided that serum potassium level is monitored.
13. Use of metformin in diabetic patients with estimated GFR < 60 mL/min/1.73 m^2 is summarized in Table 18.3.

It should be noted that none of the metformin preparations available in Poland has been licensed to use in patients with estimated GFR < 60 mL/ /min/1.73 m^2.

14. Management of diabetic patients with chronic kidney disease is summarized in Table 18.4.

Table 18.3. Recommendations for metformin use based on the severity of renal failure (according to Lipska et al., *Diabetes Care* 2011; 34: 1431–1437)

eGFR [mL/min per 1.73 m^2]	Action
≥ 60	No contraindication to metformin Monitor renal function annually
45–49	Metformin may be continued Monitor renal function every 3–6 months
30–44	Exercise particular caution when using metformin Metformin may be continued in a decreased (by 50%) dose Monitor renal function every 3 months Do not start new patients on metformin
< 30	Do not use metformin

eGFR — estimated glomerular filtration rate

Table 18.4. Management of diabetic patients with chronic kidney disease

eGFR [mL/min per 1.73 m^2]	Action
All diabetic patients	Measure albuminuria and serum creatinine and potassium annually*
45–60	Refer the patient to a nephrologist Adjust drug doses Monitor renal function every 6 months Monitor sodium, potassium*, and hemoglobin levels annually Deliver nutritional education
30–44	Monitor renal function every 3 months Monitor sodium, potassium*, and hemoglobin levels every 6 months Adjust drug doses
< 30	Refer for nephrological treatment

eGFR — estimated glomerular filtration rate

*Serum potassium levels should be particularly carefully monitored in patients treated with angiotensin-converting enzyme inhibitors/angiotensin receptor blockers/mineralocorticoid receptor antagonists, especially following significant drug dose increases

19. Diabetic eye disease

Diabetic complications involve nearly all anatomic structures of the visual system. The most common and most severe complication, with a threat of vision loss, is diabetic retinopathy and related diabetic macular edema. Among extraretinal diabetic complications, clinically the most important are diabetic cataract and secondary (hemorrhagic) glaucoma. The recommendations given below take into account the new classification of diabetic retinopathy.

Prevention, diagnosis, and management of diabetic retinopathy

I. Natural history and classification of diabetic retinopathy

1. No evidence of diabetic retinopathy.
2. Mild non-proliferative diabetic retinopathy (NPDR) — presence of microaneurysms only.
3. Moderate non-proliferative diabetic retinopathy — more advanced changes than in a mild form but less advanced than in a severe form.
4. Severe non-proliferative diabetic retinopathy:
   — Microhemorrhages (> 20) in 4 retinal quadrants; and/or
   — Venous beading in least 2 quadrants; and/or
   — Intraretinal microvascular abnormalities in at least 1 quadrant.
5. Proliferative diabetic retinopathy (PDR) (retinal neovascularization and connective tissue growth) leading to vision loss in the mechanisms of:
   — Recurrent bleeding to the vitreous body from the retinal neovessels;
   — Retinal detachment due to traction by proliferative membranes;
   — Development of glaucoma.

II. Natural history and classification of diabetic macular edema

1. No evidence of diabetic macular edema.
2. Mild diabetic macular edema — lesions away from the macular center.
3. Moderate diabetic macular edema — lesions close to the macular center.
4. Severe diabetic macular edema — lesions involving the macular center.

III. Risk factors for the development and progression of diabetic retinopathy

1. Duration of diabetes — the strongest prognostic factor for the development and progression of diabetic retinopathy
2. Poor metabolic control of diabetes:
   — Intensive treatment reduces the risk of the development and progression of retinopathy in patients with diabetes type 1;
   — Intensive treatment of diabetes type 2 reduces the rate of microangiopathic complications and reduction of HbA_{1c} level by 1% is associated with a significantly reduced risk of the development of microangiopathy.
3. Hypertension
4. Lipid disorders
5. Diabetic nephropathy
6. Pregnancy in diabetic women
7. Period of adolescence
8. Surgery for cataract
9. Following kidney and pancreas or kidney transplantation

IV. Diagnosis of diabetic retinopathy

1. Assessment of visual acuity
2. Assessment of color identification
3. Fundoscopy (using an ophthalmoscope, always with mydriasis)
4. Digital color photographs of the eye fundus used mostly for screening (they do not replace complete ophthalmologic examination)
5. Fluorescein angiography of the eye fundus
   — Indications:
   - Identification of moderate and severe preproliferative retinopathy,
   - Identification of early neovascularization foci in proliferative retinopathy,
   - Evaluation of the effectiveness of laser photocoagulation,
   - Investigation of unexplained decrease in visual acuity.
6. Wide-angle scanning laser ophthalmoscopy
7. Optical coherent tomography — major method for the diagnosis and monitoring of macular edema.
8. Ultrasound — particularly in patients with vitreous body hemorrhage.
9. Confocal microscopy (evaluation of corneal lesions as an early indicator of neuropathy)

V. Indications for ophthalmologic examination in diabetic patients

1. Initial examination
   — In diabetes type 1 — should be performed within 5 years after the diagnosis;
   — In diabetes type 2 — should be performed at the time of the diagnosis or shortly after the diagnosis.
2. Follow-up examinations and management:
   — Indicated due to an initially asymptomatic nature of retinopathy.
   — Frequency should depend on the degree of severity of diabetic retinopathy:
   - No retinopathy at baseline — once a year,
   - Early non-proliferative retinopathy — every 6 months,
   - More severe non-proliferative retinopathy — every 3 months,
   - Severe non-proliferative retinopathy — urgent laser therapy,
   - Proliferative retinopathy — urgent laser therapy or consideration of other ophthalmologic procedures (e.g. vitrectomy),
   - Diabetic macular edema — urgent laser therapy in extrafoveal disease; intravitreal anti-VEGF injections and possibly laser therapy in foveal disease,
   - Following retinal laser treatment — one month after the procedure,
   - Following vitrectomy — individualized follow-up depending on the condition of the eye fundus,
   - In pregnant diabetic women — every 1–3 months throughout the pregnancy depending on the condition of the eye fundus,
   - In women contemplating pregnancy — before conception, with retinal laser treatment at that time if needed.
3. Urgent indications for ophthalmologic examination:
   — Risk of vision loss:
   - Presence of proliferative retinopathy,
   - Presence of advanced eye complications (retinal neovascularization, vitreous body hemorrhage, acute retinal detachment);
   — Presence of changes potentially associated with a risk of vision loss:
   - Severe non-proliferative retinopathy,
   - Non-proliferative retinopathy with diabetic macular edema,
   - Other difficult-to-interpret abnormalities in the eye fundus or unexplained decrease in visual acuity,
   - Pregnancy.

Table 19.1. Recommended frequency of ophthalmologic examinations in various patient groups

Initial examination	
Diabetes type 1	**Diabetes type 2**
Initial 5 years after the diagnosis (when diagnosed during puberty — shortly after the diagnosis)	At the time of the diagnosis
Follow-up examinations and treatment	
Severity of retinopathy	**Frequency of examinations and treatment**
No retinopathy	Annually
Early non-proliferative	Every 6–12 months
Preproliferative	At least every 3–6 months
Proliferative	Urgent laser therapy
Diabetic macular edema:	
extrafoveal	Urgent laser therapy
intrafoveal	Intravitreal anti-VEGF injections + laser therapy
Follow-up after ophthalmologic procedures in special situations	
After laser treatment	Depending on the condition of the eye fundus
After vitrectomy	Depending on the condition of the eye fundus
Pregnant women	Every 1–3 months depending on the condition of the eye fundus
Women planning pregnancy	Before conception; laser therapy at that time
Uncontrolled diabetes, hypertension or proteinuria	Every 1–6 months regardless of fundoscopy findings

The recommended frequency of ophthalmologic examination in specific patient groups is summarized in Table 19.1. Following these primarily screening recommendations can reduce even several times the risk of blindness caused by diabetes.

VI. Management of diabetic retinopathy

1. Treatment intensification in patients with poor metabolic control of diabetes, intensive treatment of hypertension, primarily using ACEI and ARB, and treatment of dyslipidemia (fenofibrate, statins). Acetylsalicylic acid used for cardioprotection is not contraindicated in patients with retinopathy and does not pose a risk of retinal hemorrhage.
2. Retinal laser photocoagulation (possible if the optical system of the eye is clear):
   — Early retinal laser photocoagulation reduces progression of diabetic retinopathy;
   — Types of retinal laser photocoagulation:
   - Focal — recommended in early retinopathy and extrafoveal diabetic macular edema,
   - Grid-type — in diffuse diabetic macular edema,
   - Panphotocoagulation — recommended in severe non-proliferative and proliferative retinopathy.
3. Vitrectomy
   — Indications:
   - Vitreous hemorrhages unresponsive to other therapies; in such cases, early vitrectomy is indicated (the earlier is the procedure, the better are its outcomes),
   - Advanced complicated proliferative retinopathy.
4. In severe diabetic macular edema, intravitreal injections of anti-VEGF agents aflibercept, ranibizumab, and bevacizumab, optionally in combination with retinal laser therapy. Bevacizumab is used off-label for this purpose. Intravitreal anti-VEGF agent injections are recommended as the first-line therapy of any diabetic macular edema with foveal involvement.
5. Intravitreal or periocular injections of steroids exerting an antiangiogenic and antiedematous effect, e.g. triamcinolone, long-acting dexamethasone, or extended-release fluocinolone acetonide.
6. In irreversible vision loss, a low vision and blindness specialist should be consulted and the patient should be referred for blind rehabilitation services.

20. Prevention, diagnosis, and management of diabetic neuropathy

I. Diabetic neuropathy causes severe complaints, significantly reduces the quality of life, and is an established risk factor forthe development of diabetic foot syndrome and sudden deaths.

II. Clinical classification of neuropathy:
- — Generalized symmetrical polyneuropathy:
  - Chronic sensorimotor,
  - Autonomic,
  - Acute sensory;
- — Focal and multifocal neuropathies:
  - Involving cranial nerves,
  - Involving spinal nerves (thoracic and lumbar),
  - Focal limb neuropathies, including compression syndromes,
  - Proximal motor neuropathy (amyotrophy).

III. Approach to testing for neuropathy:
- — Testing frequency:
  - Diabetes type 1 — at 5 years after the diagnosis, unless symptoms suggesting neuropathy develop earlier,
  - Diabetes type 2 — at the time of the diagnosis,
  - Evaluation for evidence of diabetic neuropathy — at least once a year.
- — Other, non-diabetic etiologies of the peripheral nervous system damage should be excluded (following a neurological consultation).
- — In doubtful cases neurologist consultation is indicated.

IV. Diagnostic criteria of diabetic neuropathy

Somatic peripheral polyneuropathy

A. Diagnostic methods:
- — Pressure sensation using a 10 g monofilament (Semes-Weinstein 5.07);
- — Vibration sensation using a biothesiometer or 128 Hz tuning forks;
- — Pain sensation using a sterile needle;
- — Temperature sensation using a rod with two different (metal and plastic) ends;
- — Electroneurographic examination.

B. Diagnostic principles:
- — Symptoms: abnormal sensation, numbness, burning, tingling, spontaneous pain, muscle jerks and cramps, mostly involving feet and calves, persisting for several months (worsened or occurring mostly during the night; exercise does not cause or worsen symptoms);
- — Signs: reduced muscle power, reduced or absent tendon reflexes (knee, ankle), reduced or absent vibration, pressure, pain and temperature sensation;
- — Peripheral diabetic neuropathy is considered most likely based on the presence of 2 out of the following 3 components of the clinical examinations: symptoms, reduced or absent sensation (touch, vibration, pain, and/or temperature) and/or absent tendon reflexes;
- — Nerve conduction studies (electroneurography) may be also necessary to make a definite diagnosis of neuropathy in selected patients;
- — Evaluation of corneal nerve fiber density by confocal microscopy may also used for the diagnosis of thin fiber neuropathy.

Autonomic neuropathy

Autonomic nervous system function is evaluated indirectly based on the analysis of effector organ function in response to specific stimuli. Due to a non-specific nature of clinical symptoms and signs, the diagnosis should be supported by specific tests. It is necessary to exclude other disease of the effector organ, take into account other organic and functional abnormalities, and exclude an effect of the treatment used.

1. Cardiovascular system:

Autonomic neuropathy may be suspected when the results of two of the tests listed below are positive, and it may be diagnosed when the results of three tests are positive:
- — Tests evaluating the parasympathetic nervous system:
  - Heart rate change during deep breathing,
  - Heart rate change in response to the upright posture,
  - Heart rate change in response to the Valsalva manoeuver;
- — Tests evaluating the sympathetic nervous system:
  - Systolic blood pressure change in response to the upright posture,
  - Diastolic blood pressure change;
- — Other tests:
  - Evaluation of heart rate variability during a 5-minute resting ECG recording or 24-hour Holter monitoring.

2. Gastrointestinal system:
- — Gastric dysfunction — barium radiography, radioisotope scanning, electrogastrography (EGG), insulin challenge test, manometry;
- — Small intestine dysfunction — no specific diagnostic tests, manometry to identify abnormal intestinal motility;

— Large intestine dysfunction — barium follow-through, manometry;
— Gall bladder dysfunction — functional ultrasound.

3. Genitourinary system
   — Bladder dysfunction — cystometry (evaluation of bladder volume before and after micturition); bladder sphincter electromyography, uroflowmetry and urethral pressure profile;
   — Erectile dysfunction — questionnaires [International Index of Erectile Function (IIEF) and its abbreviated 5-item version (IIEF-5)], vascular studies (Doppler ultrasound), cavernosography, functional testing (nocturnal penile tumescence tests).
4. Dysfunctional sudomotor function — simple perspiration tests, testing using sophisticated equipment (evaluation of sudomotor function using Sudoscan).
5. Pupil dysfunction — pupillometry.

V. Management

1. Causal treatment of diabetic neuropathy:
   — Optimal metabolic control of diabetes, with particular attention to avoiding hypoglycemia;
   — Blood pressure and lipid control, smoking cessation, avoiding alcohol use;
   — Drug therapy: alpha-lipoic acid, benfotiamine, ACEI.
2. Symptomatic treatment of somatic diabetic neuropathy:
   — Pregabalin;
   — Gabapentin;
   — Carbamazepine;
   — Tricyclic antidepressants (amitryptiline);
   — Serotonin and norepinephrine reuptake inhibitors: duloxetine, venlafaxine;
   — Tramadol and opioid analgesics;
   — Topical agents: capsaicin, nitroglycerin;
   — Non-steroidal anti-inflammatory drugs and acetaminophen;
   — Non-drug treatments: physical therapy, acupuncture.
3. Symptomatic treatment of autonomic diabetic neuropathy:
   — Cardiovascular system:
     • Cardiac arrhythmia — controlled graded exercise, ACEI, beta-blockers (without intrinsic sympathomimetic activity),
     • Orthostatic hypotension — compression clothing to increase venous return (e.g. compression stockings), mineralocorticoids (fludrocortisone);
   — Gastrointestinal system:
     • Gastroparesis — diet modification (frequent small meals, semiliquid or liquid diet in severe dysfunction), prokinetic drugs (domperidone, cisapride, erythromycin), acid reducers (H2 receptor antagonists, proton pump inhibitors), antiemetics, nasoduodenal tube, surgical treatment, gastric electrical stimulation therapy,
     • Intestinal dysfunction — diet modifications (consider gluten- or lactose-free diet), cholestyramine, clonidine, octreotide, antidiarrheals (loperamide), pancreatic enzymes, antibiotics;
   — Genitourinary system:
     • Bladder dysfunction — avoiding urinary retention, regular micturition, anticholinergic drugs (bethanechol), external bladder massage before micturition, bladder catheterization (temporary or permanent);
     • Erectile dysfunction — phosphodiesterase type 5 inhibitors (sildenafil, vardenafil, tadalafil), central erection stimulants (apomorphine), vacuum penile pump devices, intracavernosal prostaglandin E1 injections, penile prostheses,
     • Female sexual dysfunction — mechanical stimulating devices, topic moisturizers;
   — Dysfunctional perspiration:
     • Botulinum toxin, vasodilators, moisturizing creams.

21. Diagnosis and management of diabetic foot syndrome

Multidisciplinary (reference) diabetes foot clinics should be created in regional (voivodship, university) diabetologic centers, and basic diabetes foot clinics should be created at diabetology clinics to continue care initiated in a multidisciplinary clinic.

Organizational structure and responsibilities in accordance with the Diabetes Foot Outpatient Treatment Support Program by the Ministry of Health (http://www.mz.gov.pl/zdrowie-i-profilaktyka/programy-zdrowotne/wykaz-programow/program-wsparcia-ambulatoryjnego-leczenia-zespolu-stopy-cukrzycowej/).

I. Definition. Diabetic foot is a foot infection and/or ulceration and/or deep tissue (e.g., bone) destruction caused by a varying degree of damage to peripheral nerves and/or pedal vessels. Implied in the definition is further categorization of this condition into neuropathic, vascular, and mixed diabetic foot.

Investigations in the diabetic foot syndrome include evaluation for peripheral polyneuropathy, leg ischemia, deformations, and other risk factors for foot damage. It is recommended that physicians directly inspect patients' feet during each visit.

II. Risk factors for diabetic foot syndrome:

— Peripheral neuropathy and/or vascular ischemic changes within lower limbs;
— Low patient knowledge;
— Long-lasting, poorly controlled diabetes;
— Inappropriate foot hygiene;
— Inappropriate footwear;
— Presence of corns and calluses;
— Foot deformations;
— Increased sole pressure.

Factors contributing to disease recurrences:

— Previous amputations;
— History of ulcerations;
— Neuropathic arthropathy (Charcot foot).

III. Clinical classification of diabetic foot syndrome

The Perfusion, Extent, Depth, Infection, Sensation classification (PEDIS) is recommended, taking into account both infections and the ischemic factor (Table 21.1).

IV. Prevention:

— Systematic foot examination; yearly evaluation for abnormal sensation (physical examination) and ischemia [assessment of dorsalis pedis and posterior tibial artery pulses; consider measurement of the ankle-brachial index (ABI)] in all patients;
— Regular podiatric care (removal of calluses and hyperkeratosis);
— Use of recommended footwear, orthopedic insoles, and socks;
— Systematic patient education regarding foot hygiene and consequences of absent protective pain sensation;
— Education and systematic treatment of other risk factors such as smoking, overweight, hypertension, and dyslipidemia, along with good metabolic control of diabetes;
— Early identification and treatment of limb ischemia.

V. Infections in the course of diabetic foot

1. The diagnosis is mostly based on the clinical picture (the presence of at least two typical symptoms and signs of infection) and not only microbiological testing results.
2. Evaluation of the severity of infection (see the PEDIS classification).
3. Microbiological testing (including antibiotic susceptibility) and its interpretation (colonization, contamination, infection):
   — It is recommended to collect tissue samples, aspirate, or scrapings for culture following wound debridement;
   — Testing is recommended if a clinically infected wound is present;
   — When evaluating infection, interpretation of the culture result is difficult, and it is recommended that this evaluation is primarily based on the clinical picture;
   — Blood culture is recommended only in case of systemic evidence of an infection (grade 4 by the PEDIS classification);
   — If there is no or mild clinical wound infection, and no antibiotics were used previously, it is acceptable not to perform culture.
4. Evaluation for osteomyelitis (should be performed in all cases of an infected ulceration, particularly if chronic):

Table 21.1. The PEDIS classification

	Degree of severity			
	1	2	3	4
Perfusion	Normal: palpable pedal pulses or ABI > 0.9	Clinical evidence of impaired perfusion: intermittent claudication, ABI < 0.9, $TcpO_2$ 30–60 mm Hg	Critical ischemia: resting pain, ABI < 0.4, $TcpO_2$ < 30 mm Hg	
Extent	Ulceration size in square centimeters			
Depth	Superficial ulceration within the dermis	Ulceration may involve all soft tissues	Penetration to bone: osteolysis in X-ray or positive probe-to-bone test	
Increase of infection	No clinical evidence of infection	Infection involving the skin and subcutaneous tissue, inflammation within 2 cm from the margin of the ulceration	Locally severe inflammation, beyond 2 cm from the margin of the ulceration, but no evidence of a systemic infection	Evidence of a systemic infection: fever > 38°C, heart rate > 90 bpm, breath rate > 20/min, leukocyte count > 12,000/mm^3 or < 4000/mm^3
Sensation	No evidence of sensory neuropathy in basic tests (using a monofilament and tuning forks or Neurotip)	Sensory neuropathy present		

ABI — ankle-brachial index; $TcpO_2$ — transcutaneous oxygen pressure

— Probe-to-bone test;
— Foot radiography (every 3–6 weeks);
— Magnetic resonance imaging (indicated);
— Bone biopsy or bone sample culture (indicated);
— Laboratory tests — erythrocyte sedimentation rate > 70 mm at one hour indicates an increased likelihood of osteomyelitis, and lower rates indicate a lower risk. Evaluation of C-reactive protein (CRP) level and leukocyte count may also be useful. A possibility of bone inflammation cannot be definitely excluded based on normal laboratory test results.

5. The nature of the wound (dry or exudative) is the primary criterion for the choice of dressing.

A. Approach to antibiotic therapy

— Use only for a confirmed infection (do not use prophylactically);
— Do not delay therapy.
— Initially, use an antibiotic covering the most common causative bacterial flora (staphylocci and streptococci);
— In grade 4 infections by the PEDIS classification, provide coverage also for Gram-negative bacteria and anaerobes;
— Duration of antibiotic therapy — until resolution of the infection and not just healing of the ulceration:
  • Grade 2 infection by the PEDIS classification — 1–2 weeks, in some cases longer (in particular in immunocompromised patients and those with limb ischemia);
  • Grade 3–4 infection by the PEDIS classification — 2–4 weeks;
— Route of administration:
• Intravenous — grade 4 infection by the PEDIS classification, some cases of grade 3 infection (MRSA, *P. aeruginosa*), intolerance of oral antibiotics;
• Oral — grade 2–3 infection by the PEDIS classification, improved grade 4 infections;
• Topical — collagen sponge with gentamycin; use of garamycin sponge may be considered;
• Intraarterial — not recommended.

B. Choice of antibiotics

— Severe infections:
  • Intravenous therapy — ciprofloxacin + clindamycin, amoxicillin-clavulanate or piperacillin-tazobactam, or carbapenem + vancomycin until a MRSA infection is excluded,
  • Oral continuation — amoxicillin-clavulanate and cotrimoxazole (doubled dose) or ciprofloxacin 750 mg twice daily or moxifloxacin + linezolid,
  • MRSA infection: linezolin, vancomycin;
— Less severe infections:
  • Usually oral therapy, using similar antibiotics as in severe infections, e.g.:
    • Gram-positive bacteria: semisynthetic penicillins/first-generation cephalosporins;
    • Recent antibiotic therapy, Gram-positive or Gram negative bacteria: fluorochinolones, beta-lactams or if allergy to beta-lactams: clindamycin, flurochinolones, cotrimoxazole;
— Management of osteomyelitis (no consensus treatment approach):
  • Surgical removal of the affected bone (small amputation);
  • Antibiotic therapy as in severe infections;
  • Monitoring of the treatment effectiveness: laboratory tests (erythrocyte sedimentation rate, CRP), foot radiographs.

VI. Multidisciplinary management of the diabetic foot syndrome

Effective treatment of the diabetic foot syndrome may only be provided within multidisciplinary clinics. This concept encompasses an organizational structure that allows patient access to the required specialists knowledgeable and experienced in the treatment of diabetic foot syndrome who form a therapeutic team and communicate with each other.

The management of the diabetic foot syndrome includes:

— Metabolic control of diabetes: insulin therapy (intensive insulin therapy is preferred), treatment with oral antidiabetic agents is acceptable in some cases if it allows appropriate metabolic control of diabetes and insulin treatment is not required;
— Foot off-loading: appropriate off-loading device for the affected foot (temporary footwear to offload the forefoot or hindfoot), compensatory footwear for the healthy foot, therapeutic insoles, crutches, wheelchair, plaster cast, specialized footwear, bedrest. The gold standard for foot offloading is total contact cast;
— Antibiotic therapy (oral or intravenous), see above;
— Surgical treatment — removal of necrotic tissues, drainage, incisions;
— Intravascular and vascular surgical procedures, hybrid procedures (diabetic foot with a predominant ischemic etiology — patients with low ABI and/or a history of intermittent claudication should be referred for further vascular investigations and to a vascular surgeon or angiology specialist; of note, **limb ischemia may not manifest with typical pain symptoms in many diabetic patients);**
— Podiatric treatment (regular wound care, conventional dressings, and wound moisturizing therapy);

— Other — skin transplantation; growth factors; human skin preparations (in selected cases); hyperbaric chamber, negative-pressure wound therapy; medications to improve perfusion (ischemic or predominantly vascular etiology); low-molecular-weight heparins (acute ischemia, critical limb ischemia); acetylsalicylic acid; walking training. Sulodexide treatment may be considered.

Each patient with the diabetic foot syndrome should receive education regarding ulcer prevention.

Neuropathic osteoarthropathy (Charcot foot)

— Evaluation:
  • Clinical picture when other causes have been excluded, radiograph (initially in the acute phase, followed by repeated studies), consider magnetic resonance imaging;
— Management:
  • Acute condition — off-loading for 24 hours a day (total contact cast, other forms of off-loading), bisphosphonate therapy with vitamin D and calcium administration may be considered (long-term treatment, not always effective);
  • Chronic condition — education, foot hygiene, special orthopedic footwear with corrective insoles, surgical and orthopedic procedures to correct deformations (exostectomy, arthrodesis).

Multidisciplinary team management is recommended.

VII. Indications for hospital admission

Acute admissions:
— Grade 4 infection by the PEDIS classification;
— Grade 3 infection by the PEDIS classification if intravenous antibiotic therapy is needed;
— Need for negative-pressure wound therapy;
— All cases of critical limb ischemia.

Elective admissions:
— No improvement despite 2 months of outpatient treatment;
— Preparation before planned surgery (small amputation, skin transplantation, revascularization procedures).

VIII. Amputation

— **Large amputation (above the ankle) should be considered in case of:**
  • A life-threatening condition due to inflammation, extensive necrosis (an absolute indication),
  • Debilitating, treatment-resistant pain, particularly due to ischemia (a relative indication),
  • Loss of the support function of the foot (a relative indication);
— **Small amputation (below the ankle) should be considered in case of:**
  • Liquefactive necrosis,
  • Osteomyelitis involving distal phalanges of the foot (avoidance of chronic antibiotic therapy, faster healing),
  • In dry necrosis, awaiting until autoamputation is recommended.

The choice of the level of amputation depends on tissue perfusion, and reconstruction and rehabilitation possibilities.

Amputation should always spare as much limb as possible.

22. Diabetes in children and adolescents

The following chapter deals with variations from the general recommendations related to specific pediatric issues.

I. Diabetes types in the pediatric population

1. Autoimmune diabetes type 1 is the most common form.
2. In obese subjects, impaired fasting glucose and/or impaired glucose tolerance may develop, followed by diabetes type 2. OGTT (with insulin level testing) is recommended every two years in children above 10 years of age (or earlier, if the puberty has already commenced) with BMI > 95th percentile.
3. Of note, monogenic diabetes is the second most common form of diabetes in the pediatric population in Poland. Investigations for monogenic diabetes are indicated in case of:
   — Development of diabetes during the first 9 months of life;
   — Mild hyperglycemia without the need for drug treatment;
   — Absence of anti-GAD, ICA, IA2, IAA, ZnT8 antibodies;
   — Concomitant additional structural or developmental abnormalities affecting the kidneys, liver, pancreas, brain, or presence of concomitant conditions typical for genetic syndromes associated with diabetes;
   — Presence of diabetes and/or concomitant conditions typical for genetic syndromes associated with diabetes in a first-degree relative;
   — Presence of diabetes or concomitant conditions typical for genetic syndromes associated with diabetes in a first-degree relative.

4. The number of children with cystic fibrosis and dysglycemia or diabetes is increasing. Diabetes in these patients is usually asymptomatic. Annual OGTT with blood glucose measurements at 30, 60, 90 and 120 minutes should be performed in children > 10 years of age.
5. Primary diagnostic work-up for hyperglycemia or revision of the diagnosis always includes testing for anti-GAD65 antibodies along with 1–2 from the following: ICA, IA2, IAA, ZnT8 (testing should always be performed in a reference laboratory).
6. The possibility of a mixed diabetes etiology should always be borne in mind.

II. Therapeutic targets

1. Achieving and maintaining normal, harmonious physical development including body height, weight, and composition (as evaluated using percentile growth charts), and the course of puberty that is appropriate for age and gender, and providing an appropriate quality of life of the patient and his/her family.
2. Prevention of acute and chronic diabetes complications.
3. Therapeutic targets for cardiovascular risk reduction:
   — $HbA_{1c} \leq 6.5\%$ with stable blood glucose levels and minimized hypoglycemia episodes;
   — LDL cholesterol < 100 mg/dL (< 2.6 mmol/L), HDL cholesterol > 40 mg/dL (1.1 mmol/L), triglycerides < 100 mg/dL (1.1 mmol/L);
   — Blood pressure < 90^{th} percentile for age, gender, and height (> 16 years of age: < 130/85 mm Hg);
   — BMI < 85^{th} percentile for age and gender;
   — Moderate physical activity > 1 hour per day;
   — Sedentary activities < 2 hours per day.

III. Management of diabetes

1. Drug therapy

   Diabetes type 1 — insulin therapy:
   — The approach to insulin therapy should be adjusted to individual patient needs and accepted by the patient and his/her caregivers;
   — Intensive insulin therapy is the treatment of choice, either as:
     • Multiple daily injections using insulin pen needles with the length of ≤ 6 mm,
     • Continuous subcutaneous insulin infusion (CSII) using a personal insulin pump;
   — Indications for and contraindications to CSII — see respective Chapter;
   — Initiation of CSII therapy at the disease onset is recommended in children < 10 years of age;
   — Bolus calculator function use from the beginning of the therapy is advised, as it increases the stability of blood glucose values and reduces the risk of hypoglycemia; it is necessary to verify and modify bolus calculator settings;
   — The choice of rapid-acting and long-acting insulin analogs should be individualized based on patient's needs, taking into account pharmacological differences between various preparations and their licensed indications;
   — In pediatric patients, daily insulin requirement is characterized by a large variability and increases significantly in the pubertal period;
   — During intensive insulin therapy: the magnitude of the basal dose (20–50% of the daily dose) and its profile depend on the age of the child and the type of insulin pump;
   — Rapid-acting insulin analog/short-acting insulin is best administered 15–20 or 30–45 minutes before a meal, respectively; consider dose splitting and administering half of the dose before a meal and the other half during or after a meal, and in exceptional cases administering the whole dose after a meal;
   — In appropriately educated patients, use of the bolus calculator function of the personal insulin pump increases stability of blood glucose levels and decreases the risk of hypoglycemia.

   Diabetes type 2 — metformin and/or insulin is the treatment of choice.

   In case of:
   — Absent symptoms, HbA_{1c} < 9%, and no acidosis, drug treatment may be started with metformin;
   — Present symptoms and/or $HbA_{1c} \geq 9\%$ and no acidosis, initial drug treatment includes metformin and basal insulin;
   — Ketoacidosis — initial treatment as in diabetes type 1.

   Monogenic diabetes and diabetes in genetic syndromes — treatment depends on the type of disease (use of sulphonylureas is off-label).

   Diabetes in cystic fibrosis — an insulin-dependent condition, and insulin therapy is the treatment of choice.
2. Nutrition in diabetic children and adolescents

   Basic principles of healthy nutrition in diabetic children are the same as in their non-diabetic peers.

   It is recommended to maintain normal energy balance and gradually reduce absorbable carbohydrate intake, maximally to 45–50% of the daily calorie requirement. Reduction of simple sugar intake to 10% of the daily calorie requirement is recommended, particularly in adolescents.
3. Self-monitoring:
   — Measurements of blood glucose, glucosuria and ketonemia/ketonuria and interpretation of these readings are the basis for pediatric diabetes care. Blood glucose monitoring may be undertaken by

blood glucose self-monitoring and/or real-time continuous glucose monitoring (CGM) generating messages and sound alerts without user input;
— Frequency of blood glucose measurements should be individualized but not less than 6 (usually 8–12) times per day;

Blood glucose should be measured in fasting conditions and before meals, 1–2 hours after the meal, before bedtime, and before, during and after exercise. Periodic evaluation of night-time blood glucose profile is recommended. Patients should be instructed to measure blood glucose immediately if feeling unwell.

If CGM is used, blood glucose levels should be measured using a glucose meter when making therapeutic decision or to verify the reading in case of hypoglycemia or high blood glucose values, and when clinical symptoms are inconsistent with the readings. Use of CGM requires structured diabetes education regarding appropriate expectations towards this system, proper sensor calibration, appropriate choice and programming of messages and alarm limits, and proper interpretation of current readings and blood glucose trends.

The CGM system allows more effective adjustment of insulin doses to blood glucose trends, resulting in more stable blood glucose values, a reduced number of hypoglycemia episodes, better metabolic control, and improved quality of life of patients and their caregivers. It is particularly indicated in children with hypoglycemia unawareness, frequent nocturnal hypoglycemia, and in patients < 10 years of age. In these patient groups, it is recommended to use insulin pumps integrated with CGM, with a function of automatic temporary cessation of insulin administration in case of low blood glucose values or a risk of hypoglycemia. Use of CGM requires structured diabetes education. Only frequent use of CGM is effective therapeutically.

Criteria of appropriate metabolic control of diabetes based on blood glucose self-measurements: mean blood glucose level < 140 mg/dL, standard deviation < 50 mg/dL.

Betahydroxybutyrate testing by a test strip is a more sensitive marker of ketonemia than testing for ketones in urine.

4. Therapeutic education
   — Education is a key element of diabetes management; it should always be targeted at the patient and his/her caregivers;
   — Patient and his/her parents/caregivers need initial education and regular educational reinforcements at least once in 1–2 years;
   — Educational methods and programs should be varied and adjusted to the patient's age, intellectual capabilities, and educational tasks of the parents;
   — In adolescents and young adults, particular attention should be paid to prevention of chronic diabetes complications, contraception, and addictions.
   — The process of developing self-monitoring skills should be gradual; too early or too late placement of this responsibility on children and adolescents with diabetes is associated with treatment failures;
   — Workshops and camps for children, adolescents and young adults with diabetes are a useful and effective educational tool;
   — Initiating and continuing diabetes education is a responsibility of the whole therapeutic team, with a particular role of a diabetes educator.
5. Psychological care
   — Continuous psychological care of children, adolescents and young adults with diabetes and their families is required since the disease onset;
   — Common problems include subclinical and clinical depressive syndromes, eating disorders including anorexia nervosa (particularly in adolescent girls), and other non-specific conditions (eating disorders not otherwise specified, ED-NOS);
   — Care should be provided by an experienced psychologist who is well versed with the problems of pediatric and adolescent diabetes.
   — Screening for depressive disorders should be performed in all patients every 1–2 years, and additionally in all patients with poor metabolic control of the disease.
6. Additional remarks
   — The whole patient family should be involved in the process of treating diabetes in children and adolescents, with joint discussions on therapeutic targets;
   — Patients should be encouraged to be independent and take responsibility for their treatment to a degree that is appropriate for their age, intellectual development, and emotional maturity;
   — Children > 10 years of age should be able to measure blood glucose using a glucose meter and CGM, inject insulin using a pen, and change infusion sets in personal insulin pumps and CGM sensors.

IV. Concomitant conditions in patients with diabetes type 1

— The most common conditions are autoimmune thyroiditis and celiac disease;
— Their course is usually oligo- or asymptomatic (e.g., increased blood glucose excursions, impaired growth).

V. Acute and chronic diabetes complications (see also respective chapters)

1. Acute complications:
— Hypoglycemia in children should be diagnosed when blood glucose falls below 70 mg/dL (3.9 mmol/L) or typical clinical symptoms occur; in case of hypoglycemia, glucose should be administered at about 0.3 g/kg body weight (dose depends on blood glucose values and active insulin), and blood glucose measurement should be repeated after 10–15 minutes;
— Severe hypoglycemia in children is diagnosed in case of altered consciousness and/or seizures;
— Diagnostic criteria for ketoacidosis and hyperglycemic hyperosmolar state in children are the same as in adults;
— Management of diabetic ketoacidosis in children is summarized in Figure 22.1;
— Management of hyperglycemic hyperosmolar state:
  • **Fluid therapy:** rapid initial infusion ≥ 20 mL/ /kg body weight of 0.9% saline, with next doses administered until restoration of peripheral tissue perfusion, followed by fluid replacement during 24–48 hours using 0.45% saline. The optimal rate of serum sodium reduction is 0.5 mmol/L per hour, and of blood glucose is 50–70 mg/dL per hour and no more than 90 mg/dL per hour. If blood glucose decreases by > 90 mg/dL per hour, addition of 2.5–5% dextrose should be considered after a few initial hours of hydration therapy;
  • **Insulin therapy:** insulin should be added if blood glucose does not decrease by at least 50 mg/dL per hour during appropriate fluid therapy only; initial insulin dose is 0.025–0.05 unit/ /kg/hour, with further adjustment to achieve blood glucose reduction at the rate of 50–70 mg/dL per hour;
  • **Electrolytes:** potassium, phosphorus, and magnesium deficit is higher than in diabetic ketoacidosis; potassium supplementation should be started as soon as renal function and diuresis is stabilized; intravenous administration of potassium phosphate and potassium chloride (1:1) allows adequate phosphate supplementation; phosphate administration may result in hypocalcemia; magnesium supplementation should be considered in hypomagnesemia.
2. Chronic complications:
— Regular follow-up evaluations are needed to prevent complications (Table 22.1);
— If any chronic complication is diagnosed, screening for other abnormalities (e.g., nephropathy, retinopathy, neuropathy, and macroangiopathy) is necessary;
— With persistent albuminuria, when albumin level is above the upper limit values, ACEI or ARB treatment is indicated to reduce its progression. Treatment effectiveness should be monitored with follow-up testing for albuminuria;
— ACE or ARB treatment is recommended to normalize blood pressure; treatment effectiveness should be constantly monitored, and obtaining nocturnal blood pressure reduction is indicated, as confirmed by ambulatory blood pressure monitoring;
— Management of dyslipidemia:
  • LDL cholesterol levels > 100 mg/dL (2,6 mmol/L) require improvement of blood glucose control and lifestyle modifications;
  • In children > 10 years of age, if previous attempts at making lifestyle modifications did not result in beneficial changes in serum lipids or other risk factors for atherosclerosis are present, genetic testing for LDL cholesterol receptor gene mutations and possibly statin treatment should be considered if LDL cholesterol level is > 159 mg/dL (4.1 mmol/L).

VI. Perioperative management (see respective chapter)

VII. Recommendations regarding diabetes care in children and adolescents (Table 22.1)

1. General recommendations
— Every child with new-onset diabetes should be admitted to a specialist pediatric diabetes unit, and later remain under regular specialist care in a pediatric and adolescent diabetes clinic until transition to adult diabetes care (for transition see Appendix 1);
— A 24-hour access to diabetes information for patients and their caregivers should be provided;
— Admission to a diabetes unit should be always considered with disease decompensation (HbA_{1c} > 7.0% or blood glucose excursions above 1 standard deviation, recurrent hypoglycemia).
2. Therapeutic team
— Inpatient care — per 10 pediatric diabetes beds: physicians (specialist in pediatric diabetes, specialist in pediatric diabetes and endocrinology, if unavailable: pediatrician/endocrinologist with an experience in diabetology confirmed by the voivodship diabetes consultant in diabetology or pediatric endocrinology or diabetology) — two full-time posts; nursing personnel devoted exclusively to diabetes education or diabetes educators — two full-time posts; dietitian (full post), psychologist (full post), and a social worker (1/4 post);
— Outpatient care — per a therapeutic team caring for 300 patients: specialist in pediatric diabetes (if unavailable: pediatrician), specialist in pediatric diabetes and endocrinology, if unavailable:

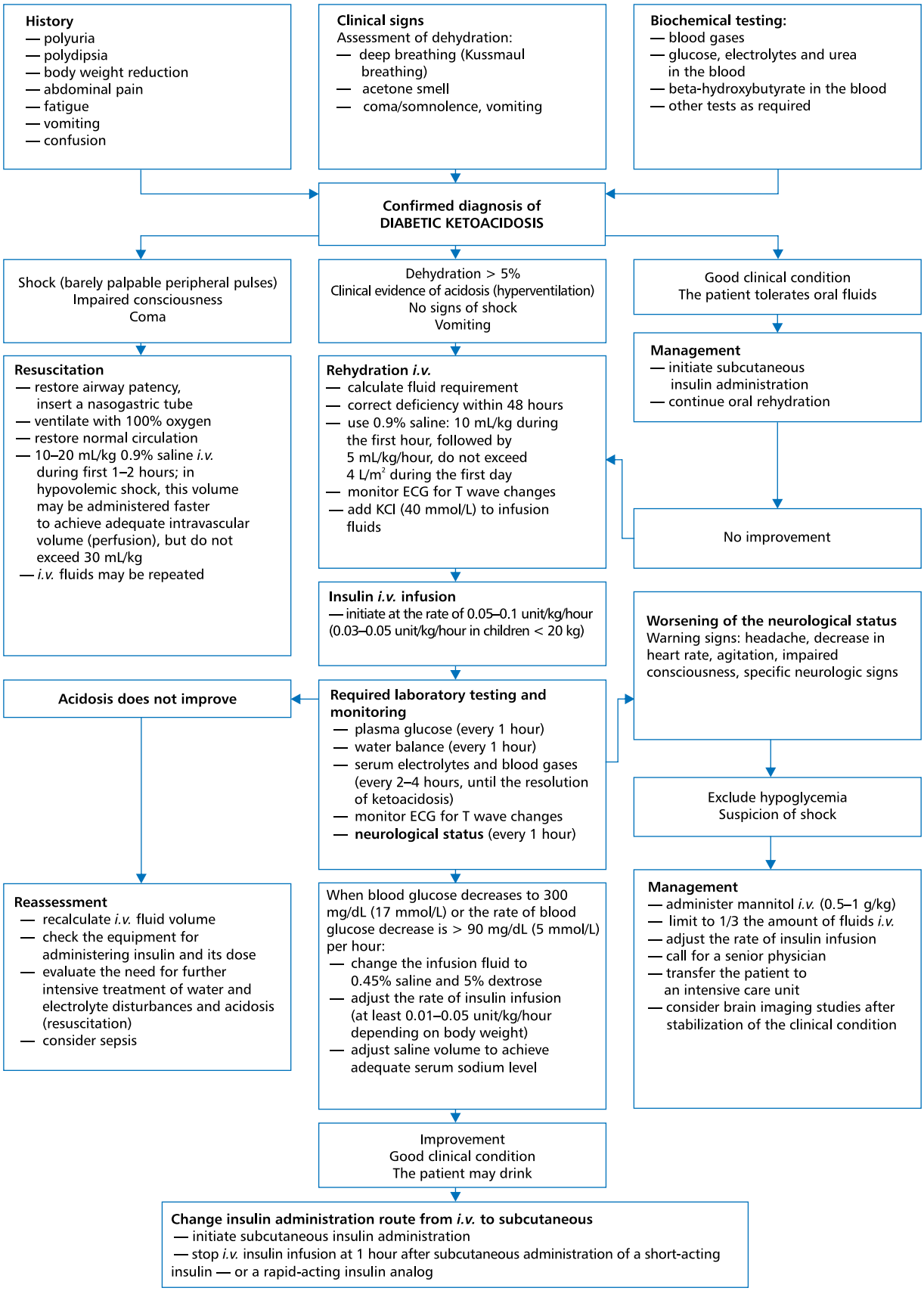

Figure 22.1. Management of diabetic ketoacidosis in children; ECG — electrocardiogram; *i.v.* — intravenous

Table 22.1. Recommendations regarding diabetes care in children and adolescents

Therapeutic education targeted at the patient and his/her caregivers	At the diagnosis and afterwards as required, at the discretion of the treating physician or education nurse
Nutritional education targeted at the patient and his/her caregivers	At the diagnosis and afterwards as required, at the discretion of the treating physician or education nurse
Psychological care of the patient and his/ /her caregivers	At the diagnosis and afterwards as required, at the discretion of the treating physician or education nurse
Anti-GAD antibodies and 2 of the following: ICA, IA2, IAA[1], ZnT8	At the diagnosis and revision of the diagnosis
HbA_{1c}	3–4 times a years, more frequently as required
Serum total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides	If positive family history — monitor annually since the diagnosis If negative family history — assess at the diagnosis, then monitor every 5 years if LDL cholesterol > 100 mg/dL (2.6 mmol/L), annually if LDL cholesterol > 100 mg/dL (2.6 mmol/L) If family history unavailable — assess at the diagnosis, then monitor every 1–2 years if LDL cholesterol > 100 mg/dL (2.6 mmol/L), every 2 years if LDL cholesterol > 100 mg/dL (2.6 mmol/L)
Serum creatinine	Calculation of eGFR using the Schwartz formula every 1–2 years, at the discretion of the treating physician
Albuminuria	Every 1–2 years, at the discretion of the treating physician. An abnormal albuminuria testing result should by confirmed by its determination in 2 of 3 subsequent urine tests
Urinalysis (sediment, proteinuria)	Every 1–2 years, at the discretion of the treating physician
Blood pressure	During each visit, at least twice a year in children < 7 years of age, 24-hour ambulatory monitoring in children > 10 years of age
Ophthalmologic examination	Every 1–2 years, at the discretion of the ophthalmologist
Body weight and growth monitoring	At each visit using percentile charts for age and gender
Monitoring of pubertal development using the Tanner scale	At the discretion of the physician, at least annually
Monitoring of menstrual bleeding	Menstrual bleeding diary
Investigations for celiac disease	According to the respective ESPGNH guidelines, screening every 1–2 years for the first 10 years of the disease duration if no clinical symptoms
Evaluation of thyroid function/ /investigations for thyroid disease	At the onset of the disease: TSH, FT4, anti-TPO and anti-TG (USG in case of positive antibody testing and/or thyroid dysfunction), followed by TSH, anti-TPO and anti-TG every 1–2 years (at the discretion of the treating physician)
Specialist consultations	According to general pediatric indication and at revision of the diagnosis

[1]Only at the diagnosis, within first 5 days of insulin therapy

pediatrician/endocrinologist with an experience in diabetology confirmed by the voivodship diabetes consultant) — one full-time post; nursing personnel with duties limited to diabetes care or diabetes educators — 1–2 full-time posts; dietician — 1/2 post; and psychologist — 1/2 post.

3. Outpatient visits
   - — Unlimited frequency of diabetes visits, recommended frequency every 6–8 weeks, at least 4 times a year;
   - — Recommended mean duration of a visit: 20–30 minutes for a specialist visit and 30–40 minutes for a procedural and diagnostic visit (treatment with a personal insulin pump);
   - — Educational visits do not always constitute a part of a physician consultation and may also be conveyed using electronic means;
   - — Additional tasks of the therapeutic team include organization of care for diabetic children in educational facilities, organization of educational camps/workshops, and preparation of educational materials.
4. Outpatient clinic and hospital unit equipment
   - — Equipment: automatic syringes, personal insulin pumps, glucose meters, CGM systems, ambulatory blood pressure monitors, ophthalmoscope, monofilaments, food scales, computer equipment to retrieve and print data from therapeutic systems;
   - — Space and necessary teaching equipment for education;
   - — Hospital units: ≥ 1 intensive metabolic care bed per 10 regular diabetes beds, equipped with pulse oximetry and ECG monitor, oxygen source, USG machine with vascular flow measurement option.

VIII. A child with diabetes in an educational facility

1. Cooperation between the therapeutic diabetes team, pedagogical personnel, school nurse, and the patient

family is needed to ensure child safety at school and prevent diabetic patient stigmatization:
- — Following the diagnosis of diabetes, the pedagogical personnel should be provided with written information about the disease and necessary help in life-threatening situations, along with contact telephone numbers of the parents, treating physician, and education nurse;
- — Appropriate training of the pedagogical personnel regarding diabetes self-management;
- — Training of the school nurse regarding the use of a glucose meter, insulin pen, or insulin pump;
- — The educational facility should be adequately provided with glucose and glucagon by the patient's caregivers;
- — Diabetes is not an indication for an individualized education plan or exemption from any activities (e.g., sport activities or school trips).

2. Duties of the pedagogical personnel:
- — Comprehensive help allowing rapid and safe patient return to the educational facility and full integration with peers;
- — Basic knowledge of diabetes self-management;
- — Allowing on-site diabetes self-monitoring in the educational facilities by patients of all age groups, with supervision by the school staff in younger children;
- — Strict cooperation with the therapeutic diabetes team and the patient's caregivers;
- — Providing immediate help in life-threatening conditions associated with diabetes.

Guidelines for teachers are available online at: http://www.mz.gov.pl/__data/assets/pdf_file/0003/6096/cukrzyca.pdf.

IX. Travel
- — Responsibilities of the patient and his/her caregivers include informing the organizer about the disease, its management, nutrition, and help in acute situations, and providing contact telephone numbers of the members of the therapeutic diabetes team;
- — An appropriate certificate in English informing about the disease should be prepared before an international travel;
- — Insulin, glucagon, glucose, glucose meter with reagent strips, equipment for insulin pumps, and insulin pens should be appropriately stored and placed in the hand-luggage.

X. Choice of future profession
- — Particular attention should be paid to education of diabetic patients, and providing them with as good education as possible;
- — A task of the therapeutic diabetes team is to help the patient with the choice of future profession by evaluating his/her health status, presence of complications, and intellectual and mental capabilities.

23. Diabetes and pregnancy

Pregnancy planning in all women with diabetes has a major effect on the course of the disease, reducing adverse maternal and fetal/neonatal outcomes.

Diabetes in pregnancy includes:
1. Pregestational diabetes mellitus (PGDM) — diabetes preexisting in a woman who becomes pregnant (regardless of the diabetes type).
2. Hyperglycemia first detected at any time during pregnancy.

I. Contraception

Diabetic women may use barrier methods or oral contraception.
1. Barrier methods [intrauterine devices (IUD), condoms] may be used with the same limitations as in non-diabetic women.
2. Hormonal contraception is possible in diabetic women:
- — Who do not smoke;
- — With BMI < 30 kg/m^2;
- — With well-controlled diabetes.

If vascular complications are present, the physician must assess the risk-to-benefit ratio before prescribing hormonal contraception.

Combined oral contraceptives containing less than 35 μg of ethinylestradiol are recommended due to their minimal effect on carbohydrate and lipid metabolism. Preferred progestins include levonorgestrel and norethisterone.

A progestin-releasing IUD is recommended as a contraceptive method in obese women > 35 years of age, patients with diabetes type 2, and in those with concomitant vascular complications.

II. Model of care for pregnant diabetic women
1. During pregnancy planning, pregnancy, and the postpartum period, all diabetic women should remain under care of an experienced team of diabetologists and obstetricians.
2. Management aims include:
- — Optimization of diabetes treatment;

— Evaluation and treatment of diabetic complications;
— Diabetes education, including nutritional advice;
— Evaluation of thyroid function (to exclude hypothyroidism): the upper limit of the reference range for thyroid-stimulating hormone (TSH) should be defined as 2.5 μIU/mL in the first trimester and up to 3.0 μIU/mL in the second and third trimester;
— During pregnancy, visits related to diabetes should occur at least once a month, and in some cases every 2–3 weeks. This is due to, among others, changing insulin requirements and the need to monitor body weight, renal function, eyesight, and blood pressure;
— In diabetic women with chronic hypertension, target systolic blood pressure is 110–129 mm Hg and target diastolic blood pressure is 65–79 mm Hg (methyldopa is the first-choice drug during pregnancy);
— In case of gestational hypertension at blood pressure values exceeding 140/90 mm Hg treatment should be resumed.

3. Pregnancy is not recommended in women with diabetes complicated by:
— Severe nephropathy with GFR < 40 mL/min;
— Uncontrolled, treatment-resistant hypertension;
— Severe, treatment-resistant proliferative retinopathy;
— Active, advanced ischemic heart disease or a history of myocardial infarction;
— Autonomic neuropathy involving the cardiac conduction system or the gastrointestinal system.

Ultimately, decisions regarding procreation are to be made by the patient herself, but the patient must be informed about the health risks of pregnancy in such cases.

Pregnancy does not seem to be associated with a risk of post-partum worsening of chronic diabetes complications. Unless the above listed complications are present, women with diabetes are free to plan any number of children they wish.

III. Diagnostic criteria and classification of hyperglycemia first detected during pregnancy

All pregnant women should be evaluated for dysglycemia. Initial fasting blood glucose measurement to detect gestational hyperglycemia should be ordered early during pregnancy, at the time of the first visit to a gynecologist. In pregnant women at risk (see Table 23.1), a diagnostic test (OGTT with 75 g of glucose) should be ordered already at the time of the first visit during pregnancy (see Chapter 1). If blood glucose is normal (see Figure 23.1), the diagnostic test should be repeated between 24 and 28 weeks of gestation or in case of symptoms suggesting diabetes. Between 24 and 28 weeks of gestation, single-step diagnostic investigation is performed using OGTT with 75 g of glucose.

Table 23.1. Risk factors for hyperglycemia during pregnancy

— pregnancy beyond 35 years of age
— history of macrosomia (birth weight > 4000 g)
— previous delivery of a neonate with a congenital anomaly
— history of intrauterine fetal demise
— hypertension
— overweight or obesity
— family history of diabetes type 2
— gestational diabetes during previous pregnancies
— multiparity
— polycystic ovary syndrome

Table 23.2. Diagnostic criteria for gestational diabetes based on an oral glucose tolerance test with 75 g of glucose according to IADPSG (2010) and WHO (2013)

Measurement	Plasma glucose	
	[mg/dL]	[mmol/L]
Fasting	92–125	5,1–6,9
60 minutes	≥ 180	≥ 10,0
120 minutes	153–199	8,5–11,0

Hyperglycemia first detected at any time during pregnancy should be diagnosed and categorized using the 2013 WHO classification:

— Diabetes mellitus in pregnancy — if general conditions for the diagnosis of diabetes are met, i.e.;
  • Fasting blood glucose ≥ 7.0 mmol/L (126 mg/dL), or
  • Blood glucose at 2 hours of OGTT with 75 g of glucose ≥ 11.1 mmol/L (200 mg/dL), or
  • Random blood glucose ≥ 11.1 mmol/L (200 mg/dL) associated with clinical symptoms of hyperglycemia;
— Gestational diabetes mellitus (GDM) — if at least one of the criteria in Table 23.2 is met.

In the postpartum period, blood glucose normalizes in most women but all women should be evaluated for dysglycemia, as diabetes in pregnancy is a risk factor for overt diabetes during later life. An OGTT with 75 g of glucose is recommended at 6–12 weeks postpartum, followed by fasting blood glucose measurements every year. An OGTT with 75 g of glucose should be performed before the next planned pregnancy.

IV. Multidisciplinary, integrated approach to the management of pregestational diabetes mellitus and hyperglycemia during pregnancy

Hyperglycemia during pregnancy increases the risk of complications in the pregnant woman and the developing fetus, and also affects further child development. Thus, blood glucose values seen in healthy pregnant

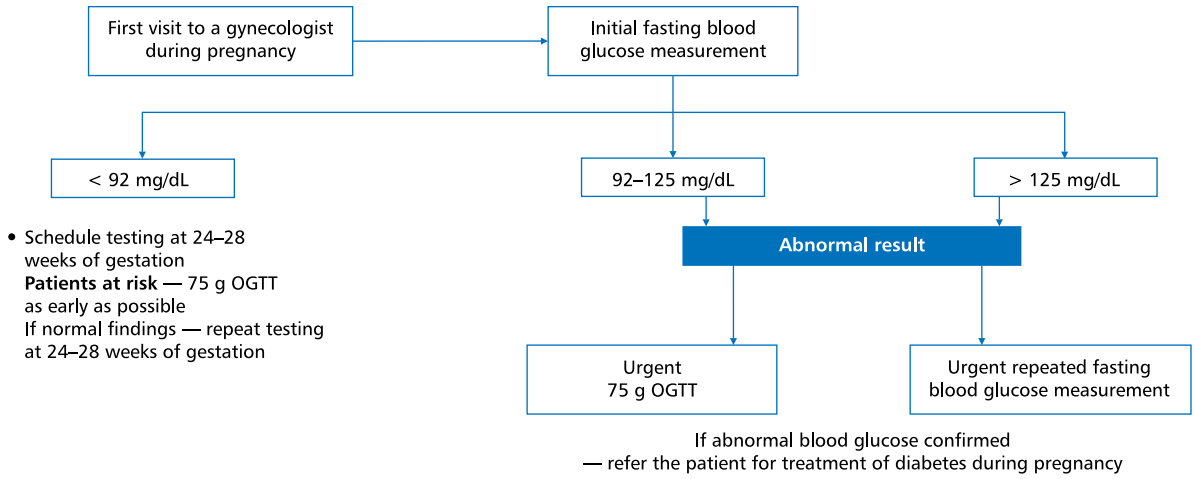

Figure 23.1. Detection of diabetes during pregnancy. An oral glucose tolerance test (OGTT) with 75 g of glucose is recommended (one step approach). Note: randomly measured fasting blood glucose in the first trimester > 92 mg/dL but > 125 mg/dL may not be used to diagnose diabetes during pregnancy; OGGT is required following appropriate patient preparation

women should be aimed for regardless of the type of pregnancy (PGDM or hyperglycemia during pregnancy). Currently, the following target self-measured blood glucose values are recommended:

— Fasting and before meals: 70–90 mg/dL (3.9–5.0 mmol/L);
— Maximum blood glucose level at one hour after a meal: < 140 mg/dL (< 7.8 mmol/L);
— Before 2 and 4 AM: 70–90 mg/dL (3.9–5.0 mmol/L).

Pregnant women should perform SBGM after an appropriate training by a nurse experienced in caring for diabetic patients. The number and timing of SBGM should depend on the severity of dysglycemia and the treatment used. CGM may be helpful in women treated with CSII.

HbA_{1c} level in women with PGDM should be measured every 6 weeks, and values < 6.5% in the first trimester, < 6.0% in the second and third trimester should be aimed for. No evidence supports the usefulness of HbA_{1c} measurements as a tool to monitor metabolic control in GDM.

1. Nutritional therapy:
   — Carbohydrates — 40–50% of the daily calorie intake (approximately 180 g carbohydrates/day); low glycemic index carbohydrates are preferred;
   — Protein — 30% of the daily calorie intake (1.3 g/kg body weight) per day;
   — Fats — 20–30% of fats the daily calorie intake (saturated < 10%);
   — Daily calorie intake depending on body weight, height, physical activity and age — the mean daily calorie requirement is about 35 kcal/kg body weight or 1500–2400 kcal;
   — Low calorie diet is recommended in overweight patients;
   — Excessive body weight in pregnant woman is associated with increased risks of large for gestational age;
   — The diet should allow normal body weight increase during pregnancy, i.e. on average by 8–12 kg depending on baseline body weight (ranging from about 7 kg for BMI > 29.0 kg/m^2 to 18 kg for BMI < 19.8 kg/m^2);
   — Use of artificial sweeteners is allowed, except for saccharin which crosses the placenta and its effect on the developing fetus is not entirely clear (see Appendix 5);
   — Use of multivitamin preparations available on the market in Poland is recommended, similarly to all pregnant women.
2. Physical exercise:
   — Aerobic activity of moderate intensity is recommended unless contraindicated.
3. Insulin therapy in PGDM:
   — Human insulins have been long used for the treatment of diabetes during pregnancy and their safety has been established. Safety of insulin analogs lispro and glargine has been shown in a number of observational studies, and that of aspart and determir also in randomized studies;
   — Intensive insulin therapy with multiple insulin injections (see Chapter 11);
   — Insulin therapy with CSII — rapid-acting insulin analogs are recommended. Patient selection for personal insulin pump therapy and managing PGDM patients using this approach should be undertaken in diabetes units experienced in CSII therapy. Treatment should be preferably initiated while planning pregnancy or during early

pregnancy (before 12 weeks of gestations), and only exceptionally later in those patients in whom adequate metabolic control cannot be achieved during treatment with multiple insulin injections.

4. Insulin therapy in hyperglycemia first detected during pregnancy:
   — The recommended approach is intensive insulin therapy with multiple insulin injections;
   — Insulin requirement is sharply reduced postpartum and insulin therapy may be withdrawn in most patients with GDM.
5. Oral antidiabetic agents are currently not recommended for the treatment of diabetes during pregnancy due to the fact that they pass through the placenta and no data are available regarding their long-term effects in the offspring. In women treated with oral antidiabetic agents, initiation of insulin therapy while planning pregnancy or as early as possible after the diagnosis of pregnancy is recommended.
6. Educational system:
   — Clinical issues — instruction provided by a physician, nurse, or dietitian knowledgeable in personal insulin pump therapy;
   — Technical issues regarding the use of a personal insulin pump — instruction provided by a nurse or physician certified as a technical instructor or an employee of the company producing personal insulin pumps;
   — Education program is undertaken according to the training card which serves to document the course of treatment;
   — Education program may be undertaken in outpatient and/or inpatient settings;
   — Treatment initiation is possible when the patient absorbs basic clinical and technical knowledge regarding CSII (understanding the therapeutic principles and technical details of using main insulin pump functions).
7. Breastfeeding should be widely promoted and recommended in women with PGDM and DGM unless contraindicated for other reasons.

24. Diabetes in the elderly

I. The prevalence of diabetes in the elderly (subjects > 65 years of age) may be as much as 25–30%.

II. Symptoms of hyperglycemia in patients > 65 years of age may be less evident than in younger subjects, leading to a delayed diagnosis.

III. Expected survival time is much reduced in diabetic patients at an advanced age, and thus it should be remembered while planning the therapy that preventing complications that develop after several years of the disease becomes less important than in younger subjects.

IV. Management goals in diabetic patients > 65 years of age:
   — The major management goal in the elderly diabetic patients is to improve or at least preserve their previous quality of life. Avoiding hypoglycemia while reducing the symptoms of hyperglycemia is of key importance;
   — If the expected survival time of a diabetic patients is longer than 10 years, diabetes control should be gradually instituted with the target HbA_{1c} level of ≤ 7%;
   — In patients at an advanced age with long-standing diabetes and significant macroangiopathic complications (previous myocardial infarction or stroke), the target HbA_{1c} level is ≤ 8.0%;
   — Investigating for diabetic complications, preventing their progression, and recommending appropriate therapy;
   — Management of concomitant conditions to reduce functional impairment and improve the quality of life.

V. Physical exercise — following initial determination of the individual risk and patient's exercise tolerance, outdoor exercise characterized by gradual onset and termination should be recommended, with avoidance of straining and breath-holding exercises and due attention to the risk of trauma, in particular the risk of developing diabetes foot syndrome.

VI. Nutritional recommendations — general recommendations apply; no age-specific recommendations; diet modifications are of little effectiveness due to long-lasting dietary habits.

VII. Oral antihyperglycemic agents:
   — Metformin — see Chapter 10, section II (stage 1 treatment of diabetes type 2); consider concomitant conditions and an increasing risk of metabolic acidosis; particular attention is required in patients with estimated GFR < 60 mL/min/1.73 m^2 (see Table 18.3);
   — Sulphonylureas — treatment should be initiated with low doses due to a risk of hypoglycemia;

— DPP-4 inhibitors, GLP-1 receptor agonists, alpha-glucosidase inhibitor, PPAR-γ agonist, SGLT-2 inhibitors — no specific contraindications exist to the use of these agents in patients > 65 years of age; these agents may be particularly useful in this age group due to a minimal risk of hypoglycemia. Do not use the PPAR-γ agonist in patients with even mild heart failure.

VIII. Insulin therapy:
— No specific indications and contraindications exist regarding insulin therapy in the elderly;
— If indicated, insulin therapy should not be delayed;
— Insulin preparations characterized by the lowest risk of hypoglycemia should be selected when initiating or modifying insulin therapy;
— Age > 65 years is not a contraindication to intensive insulin therapy;
— In some very elderly patients (> 80 years of age), it may be effective to use low doses of a short-acting insulin or rapid acting analogous of insulin before main meals without basal long-acting insulin;
— If meal size is unpredictable (e.g. patients with poor appetite or advanced dementia), rapid-acting insulin analogs administered directly after the meal in a dose adjusted to the meal size may be indicated.

IX. Diabetes education — should be targeted to both patients and their caregivers.

X. Antihypertensive therapy:
— Age is not a criterion when selecting antihypertensive drug classes;
— Benefits of antihypertensive therapy in patients > 65 years of age are similar compared to those in younger subjects.

XI. Lipid-lowering therapy:
— Although direct evidence are lacking, it may be concluded that benefits of lipid-lowering therapy seen in both primary and secondary prevention in younger subjects may also be extended to patients > 65 years of age;
— Recommended doses of statins, depending on the risk of cardiovascular disease and age of the patient, are showed in Table 13.1.

25. Preparing a diabetic patient for a surgical procedure

General remarks:
— In hospital, the patient should be consulted by a diabetologist before a surgery;
— Investigations to assess the degree of diabetes control and the presence of diabetes complications should be performed;
— Appropriate metabolic control is required in diabetic patients before the planned surgery;
— Insulin therapy must not be interrupted in patients previously treated with insulin.

I. Investigations necessary before the planned surgical procedure:
— 24-hour blood glucose profile (7 measurements during 24 hours, with an additional measurement at 3 AM in insulin-treated patients);
— HbA_{1c} level;
— Complete blood count;
— Serum creatinine, electrolytes (Na^+, K^+), aminotransferases (AST, ALT);
— International normalized ratio (INR), bleeding time, activated partial thromboplastin time (APTT);
— Acid-base balance (blood gases);
— Urinalysis;
— Fundoscopy;
— Resting ECG (see Remark 1);
— Chest radiograph.

Remark 1: Complete non-invasive diagnostic work-up (exercise testing, echocardiography, ECG Holter monitoring) should be performed in patients with several risk factors for ischemic heart disease, angina pectoris, previous myocardial infarction, heart failure, and those scheduled for an extensive procedure (e.g. abdominal or iliac vascular surgery).

Remark 2: One-day surgery may be planned only in patients with good metabolic control during intensive insulin therapy. Patients with diabetes type 2 who are effectively treated with diet only or with diet and metformin [blood glucose < 140 mg/dL (7.8 mmol/L), $HbA_{1c} \leq 6.5\%$] may also undergo one-day surgery as perioperative insulin therapy is not required in these patients. However, it is necessary to withhold metformin by at least 24 hours before the planned surgery. Other diabetic patients, regardless of the diabetes type and previous treatment, should receive insulin therapy in the perioperative period.

II. Preoperative management
1. Diabetic patients requiring intermittent insulin therapy should be admitted 2–3 days before the planned surgery.

2. Elective surgery should be delayed in patients with inadequate metabolic control [persisting blood glucose values > 250 mg/dL (13.9 mmol/L), HbA_{1c} > 9% and/ /or the presence of glucosuria with acetonuria].
3. Oral antidiabetic agents should be withdrawn 2 days before the surgery.
4. Insulin therapy with multiple injections should be initiated:
   — Daily insulin dose — 0.3–0.7 unit/kg body weight (see Remark 2);
   - 50–60% of the daily dose — a short-acting insulin or rapid-acting insulin analog administered 15–30 minutes before main meals according to the following regimen: 50–20–30% of the daily dose of short-acting insulin/rapid-acting insulin analog;
   - 40–50% of the daily dose — a long-acting insulin (NPH) administered in two doses — at 7–8 AM (40%) and 10–11 PM (60%), or a long-acting analog given once daily, most commonly in the evening. **A well-trained diabetic patient with good metabolic control is able to self-adjust insulin doses to his/her current needs and thus this practice should be allowed to be continued in the hospital instead of initiating treatment with fixed, unmodifiable insulin doses.**

Individuals using personal insulin pump should maintain the current treatment by the day of the surgery.

5. If preparation for the surgery requires a nil-by-mouth regimen during the day(s) before the surgery, intravenous infusion of 10% dextrose with 12 units of rapid-acting insulin and 10 mmol of KCl is recommended instead of meal.
6. Blood glucose control: in the perioperative period, blood glucose levels should be kept within the safe range of 100–180 mg/dL (5.6–10.0 mmol/L).
7. The surgical and anesthetic team should be informed about complications that increase the operative risk (cardiac and renal disease, neuropathy, proliferative retinopathy).

Remark 3: Temporary intensive insulin therapy is not required in patients undergoing minor procedures (tooth extraction, abscess incision, small amputation performed in the outpatient settings, cataract surgery) but only if preparation for the surgery does not require any change in nutrition. If 1 or 2 meals need to be omitted due to the surgery, intravenous glucose, insulin, and potassium infusion is recommended (500 ml of 10% dextrose with 12 units of a short-acting insulin and 10 mmol KCl), administered at the rate of 100–150 ml/hour. Insulin and potassium doses may need to be modified according to blood glucose and serum potassium levels.

III. Management on the day of the surgery

1. Use intravenous glucose, insulin, and potassium infusion with blood glucose monitoring:
   — Algorithm 1: In patients with absolute insulin deficiency, separate continuous intravenous infusions of insulin (1 unit of short-acting human insulin in 1 mL 0.9% saline) and dextrose (5––10%) using infusion pumps are recommended. For each 1 g of exogenous dextrose, 0.2–0.3 unit of insulin is needed (Table 25.1). If blood glucose during the procedure increases by 30–50 mg/dL over 180 mg/dL, the rate of insulin infusion should be increased by 1–2 units/hour. If blood glucose increases above 250 mg/dL (13.9 mmol/L), dextrose infusion should be stopped and resumed only after blood glucose decreases below 180 mg/dL (10 mmol/L). At the same time, it is also recommended to increase the rate of insulin infusion. This treatment should be continued until resumption of oral feeding. During intravenous insulin infusion, blood glucose should be monitored every 1 hour, followed by every 2 hours after blood glucose is stabilized in three subsequent readings;
   — Algorithm 2: In patients with diabetes type 2 and preserved insulin secretion, an optional approach is to administer glucose, insulin, and potassium (500 mL 10% dextrose with 8–16 units of short-acting insulin and 10–20 mmoL of KCl).
   - A larger insulin dose (≥ 16 units) should be considered in obese patients, with severe infection, during cardiac or lung surgery, in patients operated under hypothermia, and if baseline blood glucose is > 180 mg/dL (10.0 mmol/L),
   - A smaller insulin dose (12 units) should be considered in lean patients and in those receiving

Table 25.1. Dosing of 10% and 5% dextrose and insulin infusion in relation to blood glucose levels

Blood glucose	10% dextrose [mL\hour]	5% dextrose* [mL\hour]	Insulin [units\hour]
< 90 mg/dL (< 5.0 mmol/L)	50	100	Stop infusion for 15–30 minutes
90–120 mg/dL (5.0–6.7 mmol/L)	50	100	0.5–2
120–180 mg/dL (6.7–10 mmol/L)	50	100	2–3

*5% dextrose is preferred with greater fluid deficit and/or higher plasma osmolality

small insulin doses or oral antidiabetic agents before the surgery.

2. Intravenous glucose, insulin, and potassium infusion should be initiated at 8 AM and continued at the rate of 80 mL/hour until resumption of normal oral feeding.
3. During intravenous glucose, insulin, and potassium infusion, blood glucose should be kept at 100–180 mg/dL (5.6–10.0 mmol/L):
   — If plasma glucose level decreases or is close to the lower limit of the recommended range, insulin dose should be reduced by 2–4 units;
   — It is recommended to increase the insulin dose by 2 units per each 30 mg/dL (1.6 mmol/L) rise of plasma glucose level over > 180 mg/dL (> 10 mmol/L).
4. If continued surveillance over the operated patient is possible, the algorithm 1 should be preferred.

IV. Postoperative management

1. Insulin treatment with multiple subcutaneous insulin injections or using a personal insulin pump should be initiated upon resumption of oral nutrition and continued (in case of temporary insulin therapy) until surgical wound healing. Depending on blood glucose levels, insulin should be administered subcutaneously 1–3 hours before termination of the intravenous infusion.
2. If good metabolic control of diabetes was present before the surgery, resumption of previous treatment is possible upon surgical wound healing.

Remark 4: In diabetic patients previously treated with insulin, operated due to an acute or chronic inflammatory condition, a possibility of a reduction of daily insulin requirement should be taken into consideration.

Remark 5: In patients with diabetes type 2 previously treated with oral antidiabetic agents, in whom daily insulin requirement is less than 30 units, previous oral treatment may be resumed in case of good metabolic control of diabetes.

V. Perioperative management in children — Table 25.2

Insulin dosing algorithm in case of major procedures and those requiring intravenous insulin therapy (Table 25.2).

In case of non-major procedures (< 2 hours) under general anesthesia or conscious sedation, patients with good metabolic control may be admitted in the morning on the day of the procedure or in the afternoon on the preceding day. Subcutaneous insulin therapy may be continued, or the algorithm for major procedures may be used (Table 25.3).

VI. Urgent surgery

Diabetic patients may sometimes require an urgent surgery.

In these cases, it is necessary to exclude ketoacidosis associated with poor metabolic control of diabetes as the cause of peritonism. Thus, if an acute abdomen is thought to be present in a patient with diabetic acidosis (acetonuria and metabolic acidosis as indicated by blood gases), correction of acid-base abnormalities should be attempted immediately.

1. Ketoacidosis (base excess < –12; pH < 7.3) and hyperglycemic hyperosmolar state should be corrected according to the general management principles.
2. If acute diabetes complications are nor present and the patient took his/her morning insulin dose, intravenous insulin infusion should be administered during the procedure, as described above.

Table 25.2. Perioperative management in children. An algorithm for intravenous insulin dosing in relation to blood glucose levels

Infusion of a 1 unit of insulin/1 mL solution (add 50 units of insulin to 50 mL 0.9% saline) using a syringe pump		
Blood glucose [mg/dL]/[mmol/L]	**Insulin infusion rate**	**Hydration**
< 90/5.0	Stop infusion for 10–15 minutes	**Type of fluid:**
90–109/5–6.1	0.02 mL/kg/hour	• blood glucose > 250 mg/dL: 0.9% saline
110–126/6.1–7.0	0.025 mL/kg/hour (basal infusion rate)	• blood glucose < 250 mg/dL: 10% dextrose
127–143/7.0–8.0	0.035 mL/kg/hour	**Rate:**
144–216/8.0–12.1	0.05 mL/kg/hour	• 4 mL/kg/hour (for body weight up to 10 kg)
217–271/12.1–15.1	0.075 mL/kg/hour	• add 2 mL/hour per each kg of body weight between 11–20 kg
> 271/> 15.1	0.1 mL/kg/hour	• add 1 mL/hour per each kg of body weight > 20 kg Maximum rate 2000–2500 mL/day

Table 25.3. Subcutaneous insulin therapy in case of non-major procedures under general anesthesia or conscious sedation

Basal–bolus therapy	Basal insulin: NPH insulin — 50% of the morning dose, long-acting insulin analog — 100% of the morning dose
	Initiate intravenous fluids; in patients with normal blood glucose levels, non-glucose-containing fluids may be used initially, followed by 5% or 10% dextrose in amounts appropriate to prevent hypoglycemia.
	Morning procedure:
	Bolus — only as a correction dose
	Initiate intravenous fluids
	Afternoon procedure:
	Bolus — if the child is allowed to have a breakfast — the usual dose of a rapid-acting insulin analog or 50% of the usual dose of a short-acting insulin; a correction dose may be added
	Initiate intravenous fluids 2 hours before the procedure or no later than at noon
Therapy using personal insulin pump	It may be continued only if the anesthesiologist accepts this form of therapy and is able to manage it
	Continue insulin therapy using a previosly programmed basal dose for a given period during the day (modification of the basal dose is usually not required)
	Hypoglycemia: withhold basal dose administration (for up to 30 minutes)
	Hyperglycemia: a correction bolus
	Initiate intravenous fluids 2 hours before the procedure

26. Vaccinations in diabetic patients

Every child with diabetes should undergo all currently recommended vaccinations. According to the 2015 immunization schedule for Poland, compulsory immunization includes vaccination against *Streptococcus pneumoniae* at 2–5 years of age (using 10- or 13-valent pneumococcal vaccine), and 13-valent pneumococcal vaccine is recommended from 6 years of age until the elderly age. Annual influenza vaccination is recommended in children > 6 years of age and adults. Chickenpox (varicella) vaccinations should be encouraged as the disease may result in serious decompensation of diabetes.

Since 1996, all infants are vaccinated against hepatitis B virus, and since 2000 this vaccination is also offered to 14-year-olds. Vaccination is recommended in all patients. Unvaccinated subjects at any age should be actively identified and offered vaccination according to the 0, 1, 6 months regimen. If the anti-HBs antibody titer in previously vaccinated subjects is < 10 IU/L, revaccination using 1–3 doses is recommended. If a protective antibody titer is not achieved after 3 vaccine doses (at 4–12 weeks after the last dose), further vaccination is not attempted. Each vaccination should be preceded by a physician examination.

27. Recommendations regarding professional activity of diabetic patients

Developed in cooperation with Dr. Andrzej Marcinkiewicz and Prof. Jolanta Walusiak-Skorupa from the Institute of Occupational Medicine in Łódź

1. The sole fact of suffering from diabetes should never be a basis for discrimination or unequal treatment. Any professional limitations should be imposed after a careful analysis of the individual patient status and health condition.
2. In addition to providing effective therapy, the role of diabetologist in maintaining professional activity of diabetic patients includes:
   — Health education targeted at the development of health awareness and understanding of limitations arising from potential diabetes complications;
   — Help with producing an objective opinion regarding patient's health predispositions to professional activity by presenting information to the physician authorized for medical review and opining.
3. The patient's attitude should be the key factor taken into account when evaluating the health status for the purpose of professional activities. Each diabetic patient, regardless of the diabetes type and the management approach, must actively participate in the treatment.
4. Patient's health predispositions to professional activities or driving are evaluated and opined by a physician authorized to perform preventive health examinations or medically certify drivers. Due to an incidental nature of contacts with patients (often during a single consultation) leading to opining on the individual health status, it is advisable that a diabetic patient produce an opinion of the treating physician.
5. During the consultation for the purpose of medical review and opining, a diabetes specialist should:

— Evaluate patient knowledge regarding the disease, its treatment, and possible complications, rating it as extensive, satisfactory, or not satisfactory;
— Evaluate blood glucose self-management ability, rating it as high, acceptable, or low;
— Evaluate hypoglycemia awareness and the patient's ability to prevent and counteract hypoglycemia, rating it as good or not satisfactory;
— Confirm the presence or absence of hypoglycemia prodromes;
— Categorize the risk of hypoglycemia as low, acceptable, or high;
— Determine the presence of chronic diabetes complications involving the eye, nervous system, and cardiovascular system;
— Provide additional comments regarding chronic diabetes complications and the health condition of the patient which are important for the assessment of the risk for public safety.

6. Justification of professional activity limitations in diabetic patients is twofold and results from:
   — A risk of a hypoglycemic episode and associated impaired consciousness;
   — A risk of late diabetes complications which reduce the ability to engage in specific professional activities.

Contraindications to driving for holders of various categories of driving license and contraindications to work at specific workplaces are given in Appendix 2

7. Patients with advanced chronic diabetes complications should not engage in professional activities in which organ damage resulting from diabetes might affect work safety. However, this should not refrain them from undertaking other activities for which a given diabetes complication is not an issue. At the same time, the nature of professional activities and related nuisances should not hinder metabolic control of diabetes, and thus patient protection from the development and acceleration of chronic diabetes complications.
8. A diabetes consultation for the purpose of examining drivers and workers should conclude with issuing a clear opinion on a standardized diabetes consultation card, using a template provided in the Appendix 2.
9. Health requirements for diabetic patients should be divided into two categories depending on patient's professional activities or workplace.
10. The first (higher) category includes professional activities and workplaces requiring unaffected psychomotor skills and related to exposure to adverse psychosocial factors, when performing professional duties might have an effect on the safety of the worker and his/her environment (collaborators and other persons who are not directly involved in these professional activities but are present in the immediate vicinity or are potentially affected by these activities, e.g. road traffic participants, big-box store clients, etc.). More restrictive health requirements should be viewed in the context of the risk of impaired consciousness, which may be an effect of severe hypoglycemia in diabetic patients.
11. Professions requiring a higher category health requirements, and thus particularly requiring consideration of the fact that a worker suffers from diabetes, are those related to public safety, including:
    — Professional driving (passenger transport drivers, truck drivers, train and underground drivers, taxi drivers);
    — Uniformed and emergency services: armed forces (army, navy, airforce), police, fire services, municipal police, paramedic services, shipping, penitentiary service, security guards;
    — Civil aviation: pilots and aviation engineers, flight deck personnel, air traffic controllers;
    — Other professions associated with particular dangers (working at a height, operating moving equipment, work at furnaces, in high ambient temperatures, incineration plants, ironworks, mining, places with high traffic and other places with high risk of accidents).
12. The second (lower) category of health requirements involves professional activities and workplaces with noxious factors and nuisances which may have a negative effect on the course of diabetes. In case of this lower category of health requirements, some professions and workplaces should be viewed as not recommended rather than absolutely contraindicated. Thus, addition attention should be paid to, and individual evaluation of health predispositions of a diabetic patient is required when making a decision regarding initiation or continuation of work at the following workplaces:
    — requiring increased physical effort, particularly of a static nature (e.g. miner, ironworker);
    — involving shift or night work;
    — involving exposure to carbon disulfide and pesticides — 2-chlorophenoxyacetic acid derivatives (e.g. dichlorprop, mecoprop).
13. Diabetologist should serve as an advisor to young patients, in whom particular attention should be paid to the choice of profession. In these cases, the natural history of diabetes should be taken into consideration in addition to the current health status, as future health limitations may prevent not only vocational training but also, in the longer term, work itself.
14. Appendix 3 includes the Charter of Employer and Employee Rights and Duties, serving to increase patient responsibility and their position as employees on one hand, and on the other hand to counteract exclusion of the diabetic patients from the labor market.

28. Diabetes care in penitentiary institutions

Subjects detained in penitentiary institutions (prisons, remand centers, juvenile detention centers) should be offered access to the same level of medical care, including diabetes care, as in the general population.

The penitentiary institution personnel should be informed about the diagnosis of diabetes in a detained subject, and should be trained how to recognize hyper- and hypoglycemia and intervene in such situations as well as in other emergencies.

29. Metabolic surgery

Metabolic surgery is an effective approach to manage obesity and concomitant conditions, in particular diabetes type 2. Multidisciplinary approach allows proper patient selection for metabolic surgery and choice of an appropriate surgical technique.

I. Patient selection for metabolic surgery

1. Metabolic surgery should be considered in all patients with diabetes type 2 and BMI > 35 kg/m^2, especially if concomitant conditions are present, such as hypertension and lipid disorders. In particular, metabolic surgery should be considered if drug treatment and lifestyle modifications do not allow adequate control of diabetes type 2 and obesity.
2. Referral for metabolic surgery is recommended in all patients with diabetes type 2 and BMI > 40 kg/m^2.
3. Metabolic surgery is indicated in patients with diabetes type 2 between 18 and 65 years of age. The upper age limit may be in some cases extended to 70 years if the individually assessed operative risk is lower than the potential benefits of surgery.
4. Patient selection for bariatric surgery should be performed by a physician team that at least comprises a diabetologist and a surgeon with a large experience in metabolic surgery. It is also recommended that the multidisciplinary team involved in patient selection include a cardiologist, respiratory medicine specialist, psychologist or psychiatrist, anesthesiologist, and dietician.

II. Types of surgical procedures

1. It is recommended that patients be referred for minimally invasive (laparoscopic) surgery.
2. Based on the available study results, patients with diabetes type 2 should be primarily referred for laparoscopic Roux-en-Y gastric bypass, laparoscopic sleeve gastrectomy, or laparoscopic biliopancreatic diversion.
3. The decision regarding the type of surgery should be made after a surgical consultation and individual consideration of the advantages and disadvantages of all surgical techniques listed above.
4. Before making the decision regarding metabolic surgery, patients are recommended to become acquainted with the informed consent forms prepared by the Metabolic and Bariatric Surgery Section of the Polish Society of Surgeons.

III. Complications of surgical treatment of diabetes type 2

Thirty-day mortality after metabolic surgery has been estimated at 0.1–0.3%, which is identical with the mortality risk associated with laparoscopic cholecystectomy and may be categorized as low risk. The most common complications of metabolic surgery include suture line dehiscence (3.1%), surgical suite infection (2.3%), pulmonary complications (2.3%), and gastrointestinal bleeding (1.7%).

IV. Evaluating outcomes of surgical treatment of diabetes type 2

Diabetes type 2 resolves in 40–95% of patients, depending on its duration, severity of obesity, and the type of surgical procedure.

The following approach to evaluating outcomes of surgical treatment of diabetes type 2 is recommended:

1. Resolution of diabetes and concomitant conditions

The disease may be considered resolved if after cessation of drug therapy:

— HbA_{1c} level is < 6.5%;
— No hypoglycemia episodes occur in the patient;
— Total cholesterol is < 4 mmol/L, and LDL cholesterol is < 2 mmol/L;
— Triglyceride level is < 2.2 mmol/L;
— Blood pressure is < 140/90 mm Hg;
— Body weight decreased by > 15% compared to baseline, i.e. preoperative body weight.

2. Clinical improvement

The disease may be considered improved following metabolic surgery if after reduction of drug treatment used before the surgery:

— HbA_{1c} level decreased by > 20%;
— LDL cholesterol is < 100 mg/dL (< 2.6 mmol/L);
— Blood pressure is < 140/90 mm Hg.

V. Recommendations following surgical treatment of diabetes type 2

1. Each patient after surgical treatment of diabetes should remain under the care of a diabetologist and a general surgeon.
2. Continued vitamin and mineral supplementation is needed to prevent their deficiencies.

VI. Pregnancy and metabolic surgery

1. Pregnancy is allowed (i.e., becomes not contraindicated) 24 months after metabolic surgery.
2. Continued contact with the treating diabetologist is recommended before conception and throughout the pregnancy.

VII. Contraindications to metabolic surgery in patients with diabetes type 2

1. No patient acceptance for surgical treatment of diabetes type 2.
2. Alcohol or drug dependence.
3. Mental conditions that cannot be controlled with drugs.
4. High cardiovascular risk associated with the procedure.

30. Selected special situations in diabetic patients

I. Shift work

Shift work may be associated with both an increased risk of diabetes and its worse control. Hours of administration of oral hypoglycemic drugs or insulin may need to be modified.

1. Intensive self-monitoring is required in patients working in shifts, particularly during working hours.
2. Antidiabetic drugs associated with low risk of hypoglycemia and allowing greater dosing flexibility (both oral and injected, including insulin) are preferred in patients working in shifts.
3. Patients treated with insulin, particularly those with diabetes type 1, should be able to modify insulin doses during intensive insulin therapy.

II. Time zone change

Travel is not contraindicated in diabetes. Diabetic patients, particularly those with diabetes type 1 or 2 treated with insulin, should prepare for the travel, taking into account such factors as travel duration, means of transportation, time zone change (the direction of travel should also be considered, i.e., eastbound or westbound) and the climate of the destination country. Particular problems may be posed by a rapid change of the time zone (airplane travel).

1. Diabetic patients treated with insulin, particularly those with diabetes type 1, should be particularly alert during the period of adaptation to the new time zone (its duration in days equals the time difference in hours). Frequent blood glucose monitoring is necessary during this period.
2. Patients treated with basal-bolus insulin therapy flying westbound (i.e., with prolongation of the day) should administer a previously used long-acting insulin dose in the evening (new time). Possible hyperglycemia resulting from, e.g., meals consumed onboard, may be corrected with additional doses of a short-acting insulin/rapid-acting insulin analog. When travelling eastbound (i.e., with shortening of the day), it may be necessary to reduce the evening dose of long-acting insulin.
3. Patients treated with personal insulin pump do not need to adjust the pump clock or modify insulin doses when the time zone change does not exceed 2 hours. With a greater change of the time zone and a longer planned duration of stay in the new time zone, it is recommended to gradually shift basal insulin infusion by 2 hours per day.

III. Glucocorticosteroid therapy

Multiple drugs have a diabetogenic effect. One particularly important class of diabetogenic drugs are glucocorticosteroids, both due to the magnitude of their diabetogenic effect and the frequency of their use. Glucocorticosteroids mostly increase postprandial glycemia.

1. Substitution doses of glucocorticosteroids (hydrocortisone up to 20 mg/day) and inhaled glucocorticosteroids have no significant effect on carbohydrate metabolism.
2. An increased risk of steroid-induced diabetes is affected by the following factors: older age, obesity, impaired glucose tolerance, use of a high glucocorticosteroid dose, and simultaneous use of other diabetogenic medications.
3. The preferred approach to the treatment of glucocorticosteroid-induced diabetes is intensive insulin therapy (or only administration of short-/rapid-acting insulin preparations before meals, if fasting and preprandial glycemia is acceptable). No superiority of any insulin or insulin analog preparation over the others has been shown in steroid-induced diabetes.
4. In patients with diabetes type 2 treated with oral hypoglycemic drugs who require temporary glucocorticosteroid use, particularly in high doses, intensive insulin therapy is recommended.

5. In patients with diabetes type 2 receiving combined therapy with basal insulin (NPH insulin or a long-acting insulin analog), it is usually necessary to add short-acting insulin before meals.
6. In diabetic patients treated with insulin, glucocorticosteroid use is associated with an increased insulin requirement, particularly during the day.

Appendix 1
Recommendations regarding transition of patients with diabetes type 1 from pediatric to adult diabetes care

Transition from pediatric to adult diabetes care is a special period in the life of a young patient with diabetes type 1. The basic principle of this transition should be to provide continuity of care without any significant gap between termination of pediatric care and initiation of adult care. To make the transition smooth, the following recommendations should be adhered to:

1. The moment of transition from pediatric to adult diabetes care should be set individually so as not to interfere with the therapeutic process. Depending on the emotional development, family and educational situation, and other factors, the optimal age for transition of care is 16–21 years.
2. The patient should be prepared for the transition by his/her pediatrician over the period of at least one year.
3. At the last visit in the pediatric diabetes clinic, which should take place at least 6 months before the transition, the patient should be referred to an adult diabetes clinic in a coordinated effort, which should include in particular:
   — setting the date of first visit in the adult clinic by contacting in advance the clinic, its coordinator, or optimally the future treating physician;
   — providing the patient with the pediatric care discharge summary (see an attached template on page A57) which includes all relevant information regarding previous pediatric diabetic care;
   — sending (by conventional or electronic mail) complete information (including sensitive data regarding, e.g., management problems, difficult family situation, etc.) to the adult clinic;
   — informing the adult clinic (e.g., by e-mail) about termination of pediatric care and patient referral to the adult care.
4. Adult care should begin within 6 months after termination of the pediatric care.
5. It is recommended to create regional networks of cooperating pediatric and adult clinics that would develop the policy of continuous contact and patient transfer. This cooperation should include:
   — preparing, a year in advance, lists of patients to be discharged from pediatric care and regularly transferring these lists to adult care.
   — developing and accepting common medical record formats, including pediatric care discharge summary;
   — setting reliable communication channels, including by electronic means.
6. If the transition of care involves a large number of patients, it is recommended to appoint, both in pediatric and adult clinics, transition care coordinators who would manage the process of patient referral and care transition by scheduling visits, providing efficient flow of information, etc.
7. Devoting separate days for new arrivals of transitioned pediatric patients to adult clinics is not necessary but may be helpful in terms of organizing care, as these visits are much more time-consuming, particularly in patients treated with personal insulin pumps.

Developed by:
Leszek Czupryniak, Przemysława Jarosz-Chrobot, Tomasz Klupa, Małgorzata Myśliwiec, Agnieszka Szadkowska, Bogna Wierusz-Wysocka, and Bogumił Wolnik

Pediatric care discharge summary

1. Patient data*

Name and surname

Age PESEL

Address: City/town Postal code

Street House/apartment number

2. Duration of diabetes Years
3. Acidosis at the disease onset: Yes No
4. Family history of diabetes: Yes No
5. Antibody presence/titer: ICA IA-2A GADA IAA Not investigated
6. Peptide C level at the diagnosis: Fasting ng/mL Following stimulation ng/mL
   Not investigated
7. Duration of remission: No remission Remission Months
8. Treatment – conventional insulin therapy (mixed insulins)
   — Duration Years
   — Basal-bolus treatment
   • Fixed doses Years
   • Intensive insulin therapy (pen) Years
   • Intensive insulin therapy (pump) Years
9. Comments regarding current therapy: .....
10. Number of hospitalizations due to diabetes since the diagnosis
11. Reasons for hospitalization (state how many times): Acidosis Significant metabolic disturbances
    Labile diabetes Severe hypoglycemia
12. Episodes of severe hypoglycemia (state how many times)
13. Retinopathy: No Yes Severity
14. Nephropathy: No Yes Severity
15. Neuropathy: Peripheral: No Yes
    Autonomic: No Yes
16. Hypertension: No Yes / mm Hg (current blood pressure values)
    Treatment .....
17. Concomitant conditions .....
18. HbA_{1c} level: Current % Highest % Lowest %
19. Physical activity: High Participation in sport – specify which Average Low
20. Cigarette smoking: No Yes Former smoking
21. Alcohol: Yes Frequency Type of beverage No
22. Drugs: Yes Frequency Type No Occasionally
23. Eating disorders: Anorexia Bulimia
24. Cooperation with the therapeutic team: Good Poor Variable
25. Family problems (rapport with parents): Good Poor Dysfunctional family
26. School problems (ability to read, calculate)
    .....
27. Current schooling .....
    Physical job Mental job Does not attend any school Does not work
28. Additional remarks .....

....

Date *Treating physician*

*Mark or fill in as appropriate.

Appendix 2
Medical review and opining in drivers and workers with dysglycemia or diabetes

Developed in collaboration with Andrzej Marcinkiewicz, MD, and Prof. Jolanta Walusiak-Skorupa from the Institute of Occupational Medicine in Łódź

I. Medical review and opining in drivers

1. Medical review and opining in drivers with dysglycemia or diabetes is regulated by the Appendix No. 6 to the ordinance of the Minister of Health of July 17, 2014 on medical examinations of driving license applicants and drivers (Journal of Laws 2014, item 949), entitled "Detailed conditions of the medical examinations related to diabetes".
2. Based on the results of a medical examination, laboratory tests, and specialist consultations, a physician authorized to medically certify drivers evaluates the risk for traffic safety and includes it in the medical opinion.
3. According to the section 4 of the above mentioned Appendix to the ordinance of the Minister of Health, **an opinion of a diabetes specialist or another physician engaged in treating diabetes**, including a statement of no other medical contraindications to driving related to diabetes, **is obligatory in subjects:**
   — Applying for or holding a category C1, C1+E, C, C+E, D1, D1+E, D, D+E driving license, or a tram driving permit;
   — Working as road transport drivers;
   — Working as drivers of emergency vehicles or armored transportation service vehicles;
   — Driving license instructors and examiners.
4. In case of diagnostic or medical opining uncertainties, a physician authorized to examine drivers may also order a diabetes consultation if:
   — The patient has inadequate knowledge regarding diabetes, its, treatment, and possible complications;
   — The patient does not adhere to medical recommendations, in particular does not undertake blood glucose self-monitoring or does not take the prescribed drug therapy;
   — During documented blood glucose self-monitoring, more than 10% of flood glucose readings are below 70 mg/dL;
   — Metabolic control of the disease is poor (HbA_{1c} level > 8%).
5. To be considered by a physician authorized to medically certify drivers, a **diabetes consultation for the purpose of medical review and opining in drivers must conclude with issuing a diabetes consultation card** using a template provided in the Appendix No. 6 to the above mentioned ordinance of the Minister of Health of July 17, 2014 (see page A67).
6. The consulting diabetes specialist should also assess the patient's ability to drive, using the respective space provided in the consultation card. Issues related to dysglycemia may have the following effect of the final medical opinion:
   — No medical contraindications for driving:
      • **Without time constraints** resulting from the investigations for dysglycemia,
      • **With time constraints** resulting from the identified dysglycemia (consistent with a low or increased risk for traffic safety);
   — Medical contraindications for driving resulting from the identified dysglycemia:
      • **Relative**, with indication of a 6-month period after which the patient may undergo a repeated medical assessment (consistent with a high risk for traffic safety, and an option of reassessment),
      • **Absolute** medical contraindications for driving (consistent with a high risk for traffic safety and no indication of the timing of a repeated medical assessment).
7. Absolute contraindications for driving are as follows:
   — In holders of a category AM, A1, A2, B1, B, B+E, or T driving license:
      • Recurrent severe hypoglycemia (at least two episodes of severe hypoglycemia during the last 12 months),
      • Hypoglycemia unawareness;
   — In holders of a category C1, C1+E, C, C+E, D1, D1+E, D, D+E driving license, or tram driving permit, road transport drivers, emergency vehicle or armored transportation service drivers, and driving license instructors and examiners:
      • Any history of severe hypoglycemia,
      • Hypoglycemia unawareness,
      • Other diabetes-related complications that preclude driving.

8. **The consultation card is handed by the diabetes specialist to the patient who presents it to the physician authorized to medically certify drivers.** In case of a negative opinion regarding the ability to drive, it is recommended that the opining physician who referred a patient for a diabetes consultation is informed directly by the diabetes specialist.
9. **Diabetes consultation should be performed by a physician certified in diabetology or a physician with other board certification who manages diabetes in the consulted patient.**

II. Medical review and opining in workers

1. Medical review and opining in workers and persons taking up work is regulated by the ordinance of the Minister of Health of May 30, 1996 on medical examinations of workers, the extent of preventive care for workers, and issuing medical opinions for the purposes provided for in the Labour Code (Journal of Laws 1996 No. 69, item 332 with amendments).
2. A physician performing a preventive examination may extend it with a diabetes consultation and additional tests if these are considered necessary for proper evaluation of the health status of a worker or a person taking up work.
3. To serve as a useful opinion allowing an objective decision to be made based on individual patient assessment, **diabetes consultation for the purpose of preventive examination should include key information for the evaluation of health predispositions to work in specific conditions and in accordance with specific requirements.** For this purpose, it is recommended to use a diabetes consultation card based on the template provided (see page A68).
4. Based on the results of a medical examination, laboratory tests, and specialist consultations, a physician authorized to perform preventive examinations and medically certify workers issues a medical opinion regarding the absence or presence of medical contraindications to perform or take up work at a specific workplace.
5. **Absolute contraindications to perform work at workplaces associated with higher health requirements include:**
   — Recurrent severe hypoglycemia or even a single previous episode of medically unexplained severe hypoglycemia (a fall in blood glucose level leading to impaired consciousness and the need for medical intervention);
   — Hypoglycemia unawareness without prospects for an improvement, resulting from a chronic diabetes complication of vegetative neuropathy which impairs patient's ability to detect an increasing severity of hypoglycemia, and thus is not associated with an appropriate patient response to decreased blood glucose levels;
   — Advanced eye complications, mostly diabetic retinopathy or cataract with vision impairment;
   — Other advanced chronic diabetes complications;
   — An opinion of a diabetologist or a treating primary care physician which states a high risk of hypoglycemia and/or unawareness of hypoglycemia prodromes.
6. **Relative contraindications to perform work at workplaces associated with higher health requirements exist in conditions with a potential to improve, including:**
   — Lack of metabolic control of the disease ($HbA_{1c} \geq 8\%$);
   — Lacking or low blood glucose self-management ability;
   — Inadequate patient knowledge regarding diabetes, hypoglycemia, and the approaches to prevent hypoglycemia;
   — Non-compliance to physician recommendations.
7. In such cases, reassessment should be scheduled within 1–3 months.

Stamp of the healthcare unit or physician's practice

Diabetes consultation card for examining driving license applicants and drivers
(Appendix No. 6 to the ordinance of the Minister of Health of July 17, 2014 on medical examinations of driving license applicants and drivers — Journal of Laws 2014, item 949)

Patient data

Name and surname

PESEL

Personal identity card details and number in non-PESEL holders

Adress: City/town Postal code

Street House/apartment number

☐ Driving license applicant ☐ Driver

Diabetes: Date of diagnosis Type Treating physician:

Entity performing medical activities Diabetes clinic

Patient knowledge regarding the disease, its treatment, and complications: ☐ Extensive ☐ Satisfactory ☐ Not satisfactory

Blood glucose self-management ability: ☐ High ☐ Acceptable ☐ Low

Hypoglycemia awareness, ability to prevent: and counteract hypoglycemia ☐ Good ☐ Not satisfactory

Occurrence of hypoglycemia prodromes: ☐ Yes ☐ No

Risk of hypoglycemia: ☐ Low ☐ Acceptable ☐ High

☐ **Presence of chronic diabetes complications** ☐ No chronic diabetes complications

☐ Eye ☐ Nervous system ☐ Cardiovascular system

Comments regarding other diabetes complications:

.....

.....

Assessment of the ability to drive:

.....

.....

.....

Other remarks:

.....

.....

.....
Date

.....
Signature and stamp of the diabetes specialist or another physician engaged in treating diabetes

Diabetes consultation card for preventive examinations
— documentation of diabetes control by the treating physician for the purpose of evaluation of patient's health predispositions to professional activity(developed by A. Marcinkiewicz and D. Szosland)

Patient data

Name and surname

PESEL

Personal identity card details and number in non-PESEL holders

Adress: City/town Postal code

Street House/apartment number

Workplace

Noxious factors and nuisances

Diabetes: Date of diagnosis Type ☐ Treating physician: ☐ Primary care ☐ Diabetes clinic

Patient knowledge regarding the disease, its treatment, and complications: ☐ Extensive ☐ Satisfactory ☐ Not satisfactory

Blood glucose self-management ability: ☐ High ☐ Acceptable ☐ Low

Hypoglycemia awareness, ability to prevent: and counteract hypoglycemia ☐ Good ☐ Not satisfactory

Occurrence of hypoglycemia prodromes: ☐ Yes ☐ No

Risk of hypoglycemia: ☐ Low ☐ Acceptable ☐ High

☐ Presence of chronic diabetes complications ☐ No chronic diabetes complications

☐ Eye ☐ Nervous system ☐ Cardiovascular system

Comments regarding other diabetes complications:

.....

.....

Other remarks:

.....

.....

.....

.....

....

Date *Signature and stamp of the diabetes specialist or another physician engaged in treating diabetes*

Appendix 3
Charter of Employer and Employee Rights and Duties

Diabetes is a chronic metabolic disease that affects an increasing number of patients. It has been estimated that the number of subjects with diabetes in Poland is about 2.6 million people, and the disease has been identified and treated in 60% of them. The current scope of this problem and an increasing incidence of both diabetes type 1 and type 2 have very significant medical and socioeconomic consequences, and issues related to the prevention and effective treatment of diabetes and its complications are beyond the responsibility of the medical community and patients themselves.

According to the World Bank estimates, the economic burden of diabetes is second only to that of ischemic heart disease. This economic toll results not only from the costs of diagnosing and treating diabetes but also from the costs of premature termination of professional activity, including inability to work and related social benefits, as well as unemployment which is a particular problem in diabetic subjects.

Due to the fact that:

- unemployment rates among diabetic subjects are more than twice increased compared to the healthy population, and the resulting worse economic status may hinder appropriate diabetes control;
- the place of work is an important link in the process of preventing civilization disorders;

and also due to our belief that:

- drugs currently used in the treatment of diabetes, along with increasing patient awareness regarding self-management, lead to a longer and more effective preservation of a good health condition and the ability to remain professionally active;
- the sole fact of having diabetes does not automatically make the employee inferior;

Building on numerous European initiatives targeted at the prevention, early detection, and appropriate treatment of diabetes, and improvement of the quality of life of diabetic patients, including the European Parliament resolution of March 13, 2012 on addressing the diabetes epidemic in the European Union and the Copenhagen roadmap developed during the European Diabetes Leadership Forum on April 25-26, 2012;

On the eve of the 2012 World Diabetes Day, the signatories of the present document, representing the medical community, diabetes patient community, and the employers' community, postulate to write down the rights and duties of diabetic patients and their potential employers to increase patient responsibility and their position as employees on one hand, and on the other hand to counteract exclusion of the diabetic patients from the labor market.

Rights and duties of an employee suffering from diabetes

1. Each diabetic patient should be aware of the fact that effective diabetes control must take place both at home and at work.

2. At work, an employee suffering from diabetes should conform to the same principles of diabetes control as at home, i.e. periodic blood glucose monitoring, taking medications as prescribed by a physician, and adhering to the recommended meal timing and diet.
3. An employee suffering from diabetes should inform the employer about the disease and if possible, individually adjust the nature and timing of the work to allow disease control.
4. Diabetic patients should be aware of the contraindications to engage in some professions (e.g., pilot, public transport driver, working at height, work requiring extremely strenuous exercise) and should inform their employers if their professional responsibilities entail such activities.
5. An employee suffering from diabetes should inform his/her closest collaborators about the disease so as they are able to provide appropriate help in case of an episode of hyper- or hypoglycemia, and maintain continuity of work.

Rights and duties of an employer

1. Each employer should be aware that diabetes does not disqualify subjects with this disease from undertaking professional activities, and any employee discrimination due to incident or prevalent diabetes is unacceptable. Acquirement of the basic knowledge about the disease by the employer is the key to understand the situation of a diabetic patient.
2. Carrying out employer's duties, including the obligation to create safe and hygienic work environment, requires that the employer has the right to and should know which of his/her employees suffer from diabetes.
3. The employer should allow the employee suffering from diabetes to conform to the principles of controlling the disease at work and motivate him/her to a responsible behavior that guarantees the safety of the patient him-/herself and his/her collaborators.
4. If possible, the employer should provide the employee suffering from diabetes with a workplace that allows optimal disease control (e.g., option to discontinue shift work, short breaks for additional meals).
5. If possible, the employer should allow transfer of an employee with newly diagnosed diabetes to another/equivalent workplace if continuing work at the previous workplace might be associated with work safety hazards or would make controlling the disease difficult for the employee.
6. If possible, the employer should promote the healthy lifestyle at work by encouraging employees to engage in physical activity, adhere to a balanced nutrition, and undergo preventive examinations.

On behalf of the signatories
Prof. Leszek Czupryniak
President of Diabetes Poland
Warsaw, November 13, 2012

Appendix 4
Recommendations of the Polish Endocrine Society and Diabetes Poland on screening for thyroid dysfunction in diabetes type 1 and 2

Diabetes type 1

1. During each patient visit to a diabetes specialist, it is necessary to perform clinical examination targeted at thyroid disease. If thyroid dysfunction is suspected, thyroid-stimulating hormone (TSH) level should be measured.
2. It is recommended to determine TSH level and thyroid peroxidase autoantibody (TPOAb) titer in all patients with newly diagnosed diabetes type 1 and in patients with established diabetes type 1 in whom thyroid function was not evaluated previously.
3. In patients with anti-TPO antibody titer above the reference range and TSH level ≥ 2 mIU/L, free thyroxine (fT4) should be measured and TSH level measurement should be repeated annually.
4. In patients with anti-TPO antibody titer within the reference range and TSH level ≥ 2 mIU/L, TSH level should be measured every 2 years.
5. In patients with TPOAb titer within the reference range and TSH level < 2.0 mIU/L, TSH level should be determined every 5 years.
6. In patients with a positive family history of hypothyroidism due to chronic autoimmune thyroiditis, TSH level should be determined annually.
7. TSH level should be determined in diabetic patients with uncontrolled lipid parameters.
8. TSH level and TPOAb titer should be determined in any patient planning pregnancy (particularly with an adverse obstetric history).
9. TSH level and TPOAb titer should be determined in all patients at 4–8 weeks of gestation (initial obstetric visit).
10. In all patients with a history of Graves disease, TSH level and thyrotropin receptor antibody (TRAb) titer should be determined at 4-8 weeks of gestation (initial obstetric visit). In addition, TRAb titer should reevaluated at the end of the second trimester (before 22 weeks of gestation).

Diabetes type 2

1. During each patient visit to a diabetes specialist, it is necessary to perform clinical examination targeted at thyroid disease. If thyroid examination is abnormal, TSH level should be measured.
2. It is recommended to determine TSH level in all patients with newly diagnosed diabetes type 2 and in patients with established diabetes type 2 in whom thyroid function was not evaluated previously.
3. TPOAb titer should be determined in patients with TSH level ≥ 2.0 mIU/L.
4. If TPOAb titer is above the reference range, the diabetes type should be verified, primarily by measuring anti-glutamic acid decarboxylase (anti-GAD) autoantibodies.
5. In patients with TPOAb titer above the reference range and TSH level ≥ 2.0 mIU/L, fT_4 level should be measured, and TSH level should be determined annually.
6. In patients with TPOAb titer within the reference range and TSH level ≥ 2.0 mIU/L, and TSH level should be determined every 2 years.
7. In patients with TPOAb titer within the reference range and TSH level <2.0 mIU/L, TSH level should be determined every 5 years.
8. TSH level should be determined in diabetic patients with uncontrolled lipid parameters.
9. TSH level should be determined in any patient planning pregnancy.
10. TSH level and TPOAb titer should be determined in all patients at 4–8 weeks of gestation (initial obstetric visit).
11. In all patients with a history of Graves disease, TSH level and thyrotropin receptor antibody (TRAb) titer should be determined at 4-8 weeks of gestation (initial obstetric visit). In addition, TRAb titer should reevaluated at the end of the second trimester (before 22 weeks of gestation).

Source: Sowiński J, Czupryniak L, Milewicz A, Hubalewska-Dydejczyk A, Szelachowska M, Ruchała M, Lewiński A, Górska M, Siewko K, Wender-Ożegowska E, Zozulińska-Ziółkiewicz D, Junik R, Sawicka N, Gutaj P. Recommendations of the Polish Endocrine Society and Diabetes Poland for the diagnosis and management of thyroid dysfunction in diabetes type 1 and 2

Appendix 5
Position of the Polish Society of Obesity Research and Diabetes Poland on the use of low-calorie sweeteners

An increasing prevalence of overweight and obesity along with their complications, primarily diabetes type 2 and cardiovascular disease, is one of the major challenges of modern medicine. Obesity has been considered a 21st century epidemic by the World Health Organization. The epidemic of obesity is caused by lifestyle changes such as lack of physical activity and excessive consumption of highly processed high-energy-dense foods, leading to a positive energy balance.

Effective prevention and treatment of overweight and obesity together with their complications requires permanent lifestyle changes which are difficult due to numerous intrinsic and extrinsic factors that tend to decrease the motivation of a person forced to stop consuming favorite foods. **A reduction of the energy density of the available foods by changing their production technology and composition is an important component of prevention efforts at the societal level.** However, introduction of such changes requires consumer acceptance regarding the choice of low-calorie products, which in turn requires preservation of an attractive taste by the food industry. In humans, sweet taste preferences develop already in childhood, as human milk contains lactose and has a mildly sweet taste. To satisfy consumer preference for sweet taste and at the same time reduce the calorie content of foods and beverages, low-calorie sweeteners are used by the food industry.

Low-calorie sweeteners are substances with a sweet taste and the energy content of zero to few calories. As their sweet taste is very intensive, they may be added to foods in very low quantities. Currently, sweeteners are used in the production of non-alcoholic beverages, sweets, frozen desserts, yoghurts and puddings, as well as many medications.

A natural low-calorie sweetener, stevia, may be used for baking and cooking, as it is resistant to temperatures up to 200°C.

Based on safety studies and positive opinions of the European Food Safety Authority and the Panel on Food Additives and Nutrient Sources Added to Food, eleven low-calorie sweeteners are approved for use in the European Union: acesulfame K (E950), aspartame (E951), aspartame-acesulfame salt (E962), cyclamate (E952), neohesperidine dihydrochalcone (DC) (E959), saccharin (E954), sucralose (E955), thaumatin (E957), neotame (E961), erythritol (E968), and steviol glycosides (E960). According to the Regulation (EC) No. 1333/2008 on food additives, food products containing these substances should be labelled accordingly. In addition, the Regulation (EC) No. 1333/2008 specifies the maximum content of specific low-calorie sweeteners for different food product categories.

During the process of approving low-calorie sweeteners, the acceptable daily intake (ADI) in mg/kg body weight per day is also determined, defined as the amount of the substance which may be safely taken daily on a long-term basis (throughout life) without any harmful effects on the health. ADI values for specific low-calorie sweeteners are shown in Table 1.

The remaining approved substances are very rarely used by the food industry and therefore respective ADI values have not been determined.

European studies indicate that the intake of all low-calorie sweeteners is lower then their ADI.

Regarding reports of a purportedly increased risk of some neoplasms in experimental animals given saccharine, aspartame, and cyclamate, it should be emphasized that the results of recent human studies did not confirm these suggestions.

Based on these data, the **Polish Society of Obesity Research and Diabetes Poland confirm the safety of**

Table 1. Acceptable daily intake (ADI) of specific low-calorie sweeteners

Substance	Code	ADI [mg/kg body weight/day]
Acesulfame K	E950	0–15
Aspartame	E951	0–40
Cyclamate	E952	0–7
Saccharin	E954	0–5
Sucralose	E955	0–15
Neotame	E961	0–2
Steviol glycosides	E960	0–4

low-calorie sweetener use in food products and recommend substituting these substances for saccharose by overweight and obese subjects, particularly if dysglycemia (impaired fasting glucose, impaired glucose tolerance, or diabetes type 2) is also present.

Of note, a beneficial effect of low-calorie sweeteners on body weight in children and adolescents has been recently confirmed in randomized studies published in the *New England Journal of Medicine*.

A separate issue is the use of low-calorie sweeteners during pregnancy. While saccharine crosses the placenta and should not be used during pregnancy due to its unclear effects on the fetus, other low-calorie sweeteners are allowed during pregnancy.

The Polish Society of Obesity Research and the Diabetes Poland would like to draw attention of patients and physicians to the need to evaluate the energy value of the products in which low-calorie sweeteners have been substituted for sugar and which are marketed as safe for diabetic patients due to the fact that they have no significant effect on postprandial glucose and insulin levels. Despite this modification, some of these products may still be characterized by a high energy value due to their fat content and may contribute to an increase in body weight, thus worsening blood glucose control. The best way to make sure that a product in which low-calorie sweeteners were substituted for sugar is actually a low-calorie product is to compare its energy value with the energy value of a similar sugar-containing product, and to note its fat content.

The Polish Society of Obesity Research and Diabetes Poland emphasize that consumption of food products with a reduced energy value due to their low-calorie sweetener content may not be the sole lifestyle change introduced. This is only an approach to satisfy the need for sweet taste without consuming mono- and disaccharides, which may facilitate adherence to the nutritional recommendations and blood glucose control. However, another factor that plays an important role in the development of overweight and obesity along with their complications is fat intake which also needs to be reduced. It should also be emphasized that decreasing food energy value alone leads to a reduction of not only adipose tissue mass but also muscle mass. Thus, regular physical activity is required to prevent muscle mass loss (30 minutes of aerobic exercises at least 5 times a week, e.g. walking, cycling, swimming).

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President of the Polish Society of Obesity Research

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Appendix 6
Recommendations on personal insulin pump treatment reimbursed by the National Health Fund in diabetic children, adolescents, and young adults below 26 years of age

Developed in cooperation with Andrzej Gawrecki, MD

I. Requirements for centers providing the service reimbursed by the National Health Fund which includes patient education regarding continuous subcutaneous insulin infusion, providing the patient with an insulin pump, and offering consultation services.

1. **Initial training should include technical aspects of insulin pump handling and discussion of the following issues:** principles of basal rate programming and modification, temporary changes of a basal rate, use of simple, extended, and complex boluses, use of bolus calculator function, principles of setting up an infusion set (including choice of the puncture site). If a pump with continuous glucose monitoring option is needed, the training should also include the principles of system functioning, its calibration, interpretation of messages and alerts, and placing a sensor. Training should continue until the patient is well versed with practical aspects of personal insulin pump use.
2. **Particular attention should be paid to the following issues:** what to do in case of an insulin pump failure – return to treatment using insulin pens, management of initial symptoms of ketoacidosis, principles of withholding insulin infusion in special situations (e.g., following sport activities).
3. **Organizational requirements:** minimum duration of training 9 hours, split into minimum 3 sessions. Training should be performed in groups not larger than 6–8 persons. Parents or legal guardians should participate in training of children and adolescents. Patients should be offered an opportunity to practice with infusion sets using phantoms. It is also recommended to practice subcutaneous insertion of an infusion set in the period before initiating treatment with continuous subcutaneous insulin infusion.

The center providing reimbursement bears responsibility for appropriate training and initial insulin pump settings. These settings should also include initiation of the bolus calculator function.

In case of insulin pumps with continuous glucose monitoring option, alarm presetting is recommended, taking into account the current level of metabolic control and patient capabilities. Patient knowledge should be verified using a diabetes knowledge test developed by the Polish Diabetes Society (PTD).

Regular use of the software for insulin pump and glucose meter data retrieval is required.

II. Indications for reimbursement by the National Health Fund of personal insulin pump purchase in diabetic children, adolescents and adults below 26 years of age.

1. Early morning hyperglycemia in patients with diabetes type 1 following the end of a remission period*.
2. Frequent hypoglycemia episodes in patients with diabetes type 1 following the end of a remission period*:
   — Severe hypoglycemia episodes more frequently than once a year;
   — Hypoglycemia ≤ 70 mg/dL without the need for help of another person ≥ 4 times a week;
   — Inability to achieve target hemoglobin A_{1c} (HbA_{1c}) level without frequent hypoglycemia episodes, i.e. ≥ 4 times a week;
   — Impaired awareness of typical hypoglycemia symptoms.
3. Persistently elevated HbA_{1c} level > 6.5% but < 9.0% despite treatment intensification in a patient who is well educated regarding the principles of intensive insulin therapy, cooperates with the diabetes treatment team, and adheres to blood glucose self-monitoring recommendations (≥ 6 blood glucose measurements per day).
4. Subjects engaged in shift work, with irregular school or professional activity, or traveling frequently to other time zones, with HbA_{1c} level < 9.0%.
5. Subjects engaged in competitive sport or undertaking regular intensive physical activity, with HbA_{1c} level < 9.0%.
6. Children below 10 years of age with diabetes type 1.
7. Continuation of previous treatment with personal insulin pump if no contraindications exist (e.g., personal insulin pump failure)**.

In selected cases, the decision on insulin pump purchase reimbursement may be made by the voivodship diabetes consultant after reviewing the patient's medical records and obtaining an opinion of the treating diabetes specialist (including such issues as concomitant conditions and corticosteroid treatment).

III. Contraindications for reimbursement of personal insulin pump purchase in diabetic children, adolescents and adults below 26 years of age.

1. HbA_{1c} level ≥ 9.0% — an average value during the last year.
2. Mental disorders — psychosis and severe depression, also those affecting the parents of children below 10 years of age.
3. Intellectual disorders, also those affecting the parents of children below 10 years of age, which prevent understanding the principles of intensive insulin therapy and personal insulin pump handling.
4. Eating disorders.
5. Addiction, also those affecting the parents of children below 10 years of age.
6. Unexplained missing visits to a diabetes clinic (attendance at only one visit or no visits during a year).
7. Non-adherence to or non-comprehension of the principles of intensive insulin therapy (no adequate blood glucose self-monitoring, failure to test for ketone bodies in cases of prolonged hyperglycemia, imprecise estimation of prandial insulin doses).
8. More than one episode of ketoacidosis during a year.
9. Severe, rapidly progressing proliferative retinopathy before or during laser therapy.
10. No disease acceptance despite full diabetes care and psychologic support (a written opinion of psychologist experienced in diabetes care).
11. Poor personal hygiene.
12. Regular exposure to strong magnetic fields.

IV. Contraindications to continuation of treatment with a personal insulin pump and equipment reimbursement* in diabetic children, adolescents and adults below 26 years of age**

1. No improvement or worse metabolic control of diabetes after one year of treatment using a personal insulin pump.
2. More than one episode of diabetic ketoacidosis during a year.
3. More episodes of severe hypoglycemia compared to during treatment with insulin pen devices.
4. Non-adherence to the principles of intensive insulin therapy (< 70% of correct answers in the test to check diabetes knowledge developed by Diabetes Poland).
5. Severe skin reactions at the site of infusion set implantation despite an attempt to change the type of the infusion set.
6. Irregular exchanges of infusion sets (less frequently than every 3 days).
7. Unexplained missing visits to a diabetes clinic (attendance at only one visit or no visits during a year).
8. Persisting HbA_{1c} level ≥ 9.0% (two subsequent readings).

A diabetes specialist applies for reimbursement of personal insulin pump purchase for the patient to a center providing this service.

The patient presenting to a center offering the reimbursed service submits:

- A reimbursement application filled in by the treating diabetes specialist;
- A glucose meter report covering the last 4 weeks — at least 6 measurements per day are required (glucose meter may be read in the clinic);
- In some patients with inadequate metabolic control, providing additional information regarding the amount of consumed carbohydrate equivalents and insulin doses is indicated before considering CSII therapy. This information may be provided using a self-control diary or appropriate application (electronic data).

*Remission criteria according to Schölin A et al. *Diabet Med.* 2011; 28: 156: normoglycemia in blood glucose profile with insulin requirement < 0.3 unit/kg body weight per day and peptide C level > 0.5 ng/mL.

**Patients previously treated with a personal insulin pump which failed or reached its end of service life date undergo the same selection process as new patients. Previous treatment with a personal insulin pump does not automatically lead to reimbursement of a new device.

***An order for personal insulin pump supplies may be issued only by a physician working in a diabetes clinic or a hospital unit.

Specification of personal insulin pumps — 2016 Diabetes Poland recommendations. Necessary requirements

Developed in cooperation with Andrzej Gawrecki, MD

Issue/subject		Children < 6 years of age	Children > 6 years of age and adults
Pump stopped		Pump stop warning alarm	Pump stop warning alarm
Pump blockade		Electronic input key blockade	Electronic input key blockade
Bolus programming	Simple/standard bolus	Precision not less than 0.1 unit/bolus	Precision not less than 0.1 unit/bolus
	Extended/square wave bolus	Precision not less than 0.1 unit/bolus	Precision not less than 0.1 unit/bolus
		Maximum duration of a bolus — not less than 7 hours	Maximum duration of a bolus — not less than 7 hours
	Complex/double/multiwave bolus	Precision not less than 0.1 unit/bolus	Precision not less than 0.1 unit/bolus
Temporary change of a basal rate	Settings:	Possible percent or absolute (in units) increase or decrease of a basal rate, every 30 minutes with an automatic return to previous settings after the programmed time	Possible percent or absolute (in units) increase or decrease of a basal rate, every 30 minutes with an automatic return to previous settings after the programmed time
	Information about the current basal rate	Available on the main screen or retrieved using a single key	Available on the main screen or retrieved using a single key
	Time	Up to 24 hours	Up to 24 hours
Basal rate programming	Entering hourly doses (units/hour)	Precision not less than 0.05 unit/hour	Precision not less than 0.05 unit/hour
		At least two additional profiles of the basal rate, with a possibility of an advance programming, recalling from the device memory, and activation	At least two additional profiles of the basal rate, with a possibility of an advance programming, recalling from the device memory, and activation
Pump memory	History of boluses, alarms, basal rate, temporary changes of a basal rate, infusion set primings; software for pump data retrieval should also be able to retrieve data from a glucose meter with reagent strips eligible for reimbursement at the date of the tender, and integrate data from both sources	Minimum 30 days using a computer software and a reading device	Minimum 30 days using a computer software and a reading device
		Company provides the diabetes treatment unit with free software and equipment for data retrieval into a computer — software requirements specified in Appendix 1	Company provides the diabetes treatment unit with free software and equipment for data retrieval into a computer — software requirements specified in Appendix 1
		Information available directly on the pump:	**Information available directly on the pump:**
		Current basal rate, minimum last 20 boluses (dose and type), mean daily doses over the last 30 days	Current basal rate, minimum last 20 boluses (dose and type), mean daily doses over the last 30 days
Bolus calculator which is an integral element of the insulin infusion system (function available in the insulin pump or by wireless communication with the pump		Possibility of setting several time periods and switching between settings:	Possibility of setting several time periods and switching between settings:
		Grams or carbohydrate exchanges (carbohydrate intake); bolus calculator with an active insulin time function which reduces only the correction bolus, with duration of insulin action set by the user	Grams or carbohydrate exchanges (carbohydrate intake); bolus calculator with an active insulin time function which reduces only the correction bolus, with duration of insulin action set by the user
		Possibility of manually entering a blood glucose reading to the bolus calculator or communication with a glucose meter with reagent strips eligible for reimbursement at the date of the tender	Possibility of manually entering a blood glucose reading to the bolus calculator or communication with a glucose meter with reagent strips eligible for reimbursement at the date of the tender

Automatic infusion set primings	Yes — unlimited number of infusion set primings during the day, activated directly using a pump function	Yes — unlimited number of infusion set primings during the day, activated directly using a pump function
Infusion sets	Needles — metal (stiff) and plastic (elastic), all types covered by reimbursement	Needles — metal (stiff) and plastic (elastic), all types covered by reimbursement
	Tubing length — at least 2 lengths available	Tubing length — at least 2 lengths available
Servicing	24-hour telephone contact with an authorized helpline (knowledgeable on pump functioning, including all possible alarms and error messages) subjected to customer assessment	24-hour telephone contact with an authorized helpline (knowledgeable on pump functioning, including all possible alarms and error messages) subjected to customer assessment
	Webpage with information specified in Appendix 2	Webpage with information specified in Appendix 2
	Pump replacement within 24 hours (on workdays)	Pump replacement within 24 hours (on workdays)
	Pump shipping costs borne by the company	Pump shipping costs borne by the company
Batteries — pump power supply	Batteries: widely available (size AA, AAA batteries) at retail outlets, gas stations, newsagent's shops, home appliance stores, pharmacies, etc.	Batteries: widely available (size AA, AAA batteries) at retail outlets, gas stations, newsagent's shops, home appliance stores, pharmacies, etc.
	Sound alarm and a warning displayed on the device screen if battery power level is below 30%	Sound alarm and a warning displayed on the device screen if battery power level is below 30%
Additional accessories necessary to use personal insulin pump	Additional accessories for personal insulin pump which must be regularly replaced as per the pump manual are provided free by the manufacturer for the duration of the period of pump use (does not apply to infusion sets, insulin containers, batteries, insulin pump case)	Additional accessories for personal insulin pump which must be regularly replaced as per the pump manual are provided free by the manufacturer for the duration of the period of pump use (does not apply to infusion sets, insulin containers, batteries, insulin pump case)
Warranty period	At least 4 years for the pump; in case of malfunction	At least 4 years for the pump; in case of malfunction
	Replacement with a new pump with the warranty period not shorter than originally specified	Replacement with a new pump with the warranty period not shorter than originally specified
Menu	Full menu in Polish	Full menu in Polish
User manual	Full user manual in Polish, must describe all messages displayed by the pump	Full user manual in Polish, must describe all messages displayed by the pump
Continuous glucose monitoring (CGM) system which is an integral part of the insulin pump system (applies to insulin pumps with CGM option)	**In patients with frequent hypoglycemia episodes and/or hypoglycemia unawareness**	**In patients with frequent hypoglycemia episodes and/or hypoglycemia unawareness**
	Option of automatic interruption of basal insulin infusion by the CGM system	Option of automatic interruption of basal insulin infusion by the CGM system

Specification of personal insulin pumps — 2016 Diabetes Poland recommendations. Recommended/additional requirements

Issue/subject	Children < 6 years of age	Children > 6 years of age and adults
Reminder about the need to replace infusion set	Alarm informing about the need to replace infusion set	Alarm informing about the need to replace infusion set
History of infusion set primings	To be checked directly in the device memory	To be checked directly in the device memory
IPX 8 standard	IPX 8	IPX 8
Additional device to read pump memory at home and transmit data to the physician	Reader and software	Reader and software
Additional basal rate profiles	More than 3	More than 3
Bolus calculator	User settings: mg/dL or mmol/L (blood glucose readings) Possibility of manually entering a blood glucose reading to the bolus calculator	User settings: mg/dL or mmol/L (blood glucose readings) Possibility of manually entering a blood glucose reading to the bolus calculator
Continuous glucose monitoring (CGM) system	CGM system integrated with the insulin pump or an additional supporting CGM device	CGM system integrated with the insulin pump or an additional supporting CGM device

Appendix 1

Requirements for the computer software for pump memory data retrieval:

— Current basal rates (all available at single data retrieval, with data on graphs or in tables, exact doses and time with accuracy of insulin administration at a given basal rate);
— Used correction factors with time periods set in bolus calculators;
— History of boluses (precise information on bolus type, dose, and timing of administration);
— History of infusion set primings;
— Daily graphs showing:
  • Basal rate on a given day,
  • Temporary changes of the basal rate,
  • Timing of pump switching on and off,
  • All administered boluses, with information on their types and timing of administration, included that of extended boluses,
  • Blood glucose readings transmitted from a compatible glucose meter;
— History of alarms;
— Free provision of the software to the patients upon request;
— Data retrieval software should also be able to retrieve data from a glucose meter and integrate both types of information.

Appendix 2

Required information available on the webpage:

— Telephone number of a 24-hour helpline providing information to insulin pump users in case of technical problems associated with pump use;
— Telephone numbers of local representatives with their working hours;
— Data on pump supplies (types of needles, syringes, batteries along with their pricing etc.).

RECOMMENDED ADDITIONAL OPTIONS

1. Integration with a glucose meter: wireless communication with at least one type of a glucose meter, possibility to activate and deactivate the option of data transmission from the glucose meter to the pump, possibility of recording blood glucose values with the bolus calculator function switched on or off.
2. Insulin pumps that have a dedicated glucose meter should be distributed together with that glucose meter.
3. Alarms to remind about boluses or blood glucose measurements at times set by the user.
4. Price of infusion sets not exceeding the monthly reimbursement limit in persons <26 years of age and 30% of that limit in persons > 26 years of age.

For a separate package for children/adults with recurrent hypoglycemia: personal insulin pump and a CGM system:

— At least 1 transmitter for 5/10 pumps and 2 sensors for each transmitter.

ADDITIONAL NOTES

The ordering party may determine additional parameters in accordance with the needs of specific patient groups. In addition, the offer should include accessories necessary for therapy initiation and educations: serters, various types of infusion sets, insulin containers, batteries for the pump, protective cases.

When evaluating a pump during a tender, the pump price should count for 60%, and additional functions for 40% of the overall assessment.